

Exhibit A

Benjamin G. Neel, M.D., Ph.D.

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IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF NEW JERSEY

- - -

IN RE: JOHNSON & :
JOHNSON TALCUM POWDER :
PRODUCTS MARKETING, :
SALES PRACTICES, AND : NO. 16-2738
PRODUCTS LIABILITY : (FLW) (LHG)
LITIGATION :
:

THIS DOCUMENT RELATES :
TO ALL CASES :

- - -

March 19, 2019

- - -

Videotaped deposition of
BENJAMIN G. NEEL, M.D., Ph.D., taken
pursuant to notice, was held at Skadden
Arps, Four Times Square, New York, New
York, beginning at 8:56 a.m., on the
above date, before Michelle L. Gray, a
Registered Professional Reporter,
Certified Shorthand Reporter, Certified
Realtime Reporter, and Notary Public.

- - -

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Benjamin G. Neel, M.D., Ph.D.

<p style="text-align: right;">Page 2</p> <p>1 APPEARANCES:</p> <p>2</p> <p>3 BEASLEY ALLEN, P.C.</p> <p>4 BY: MARGARET M. THOMPSON, M.D., ESQ.</p> <p>5 BY: P. LEIGH O'DELL, ESQ.</p> <p>6 218 Commerce Street</p> <p>7 Montgomery, Alabama 36104</p> <p>8 (334) 269-2343</p> <p>9 Margaret.thompson@beasleyallen.com</p> <p>10 leigh.odell@beasleyallen.com</p> <p>11</p> <p>12 - and -</p> <p>13</p> <p>14 LEVIN PAPANTONIO THOMAS</p> <p>15 MITCHELL RAFFERTY & PROCTOR, PA</p> <p>16 BY: CHRISTOPHER V. TISI, ESQ.</p> <p>17 316 South Baylen Street,</p> <p>18 Suite 600</p> <p>19 Pensacola, Florida 32502</p> <p>20 (888) 435-7001</p> <p>21 Ctisi@levinlaw.com</p> <p>22 - and -</p> <p>23</p> <p>24 NAPOLI SHKOLNIK, PLLC</p> <p>BY: ALASTAIR J.M. FINDEIS, ESQ.</p> <p>400 Broadhollow Road, Suite 305</p> <p>Melville, New York 11747</p> <p>(631) 224-1133</p> <p>afindeis@napolilaw.com</p> <p>- and -</p> <p>RESTAINO LAW, LLC</p> <p>BY: JOHN M. RESTAINO, JR., DPM, ESQ.</p> <p>130 Forest Street</p> <p>Denver, Colorado 80220</p> <p>(303) 839-8000</p> <p>Jrestaino@restainolaw.com</p> <p>Representing the Plaintiffs</p>	<p style="text-align: right;">Page 4</p> <p>1 APPEARANCES: (Cont'd.)</p> <p>2</p> <p>3 SEYFARTH SHAW, LLP</p> <p>4 BY: THOMAS T. LOCKE, ESQ.</p> <p>5 975 F Street, NW</p> <p>6 Washington, D.C. 20004</p> <p>7 (202) 463-2400</p> <p>8 tlocke@seyfarth.com</p> <p>9 Representing the Defendant, PCPC</p> <p>10</p> <p>11 ALSO PRESENT:</p> <p>12</p> <p>13 VIDEOTAPE TECHNICIAN:</p> <p>14 Henry Marte</p> <p>15</p> <p>16</p> <p>17</p> <p>18</p> <p>19</p> <p>20</p> <p>21</p> <p>22</p> <p>23</p> <p>24</p>
<p style="text-align: right;">Page 3</p> <p>1 APPEARANCES: (Cont'd.)</p> <p>2</p> <p>3 DRINKER, BIDDLE & REATH, LLP</p> <p>4 BY: SUSAN M. SHARKO, ESQ.</p> <p>5 600 Campus Drive</p> <p>6 Florham Park, New Jersey 07932</p> <p>7 (973) 549-7000</p> <p>8 susan.sharko@db.com</p> <p>9 - and -</p> <p>10 DRINKER BIDDLE & REATH, LLP</p> <p>11 BY: KATHERINE MCBETH, ESQ.</p> <p>12 One Logan Square,</p> <p>13 Suite 2000</p> <p>14 Philadelphia, Pennsylvania 19103</p> <p>15 (215) 988-2706</p> <p>16 katherine.mcbeth@db.com</p> <p>17 Representing the Defendants, Johnson</p> <p>18 & Johnson entities</p> <p>19</p> <p>20 TUCKER ELLIS, LLP</p> <p>21 BY: MICHAEL C. ZELLERS, ESQ.</p> <p>22 515 South Flower Street,</p> <p>23 42nd Floor</p> <p>24 Los Angeles, California 90071</p> <p>(213) 430-3301</p> <p>Michael.zellers@tuckerellis.com</p> <p>- and -</p> <p>TUCKER ELLIS, LLP</p> <p>BY: JAMES W. MIZGALA, ESQ.</p> <p>233 South Wacker Drive,</p> <p>Suite 6950</p> <p>Chicago, Illinois 60606</p> <p>(312) 624-6307</p> <p>james.mizgala@tuckerellis.com</p> <p>Representing the Defendant, PTI</p> <p>Royston LLC and PTI Union LLC</p>	<p style="text-align: right;">Page 5</p> <p>1 - - -</p> <p>2 I N D E X</p> <p>3 - - -</p> <p>4</p> <p>5 Testimony of:</p> <p>6 BENJAMIN G. NEEL, M.D., Ph.D.</p> <p>7 By Dr. Thompson 12</p> <p>8</p> <p>9</p> <p>10 - - -</p> <p>11 E X H I B I T S</p> <p>12 - - -</p> <p>13 NO. DESCRIPTION PAGE</p> <p>14 Neel-1 Notice of Deposition 16</p> <p>15 Neel-2 Expert Report 18</p> <p>16 Of Benjamin G. Neel</p> <p>17 MD, Ph.D.</p> <p>2/25/19</p> <p>18 Neel-3 Materials 19</p> <p>19 Considered List</p> <p>20 Neel-4 Appendix A 53</p> <p>21 GWAS Associations</p> <p>22 For Ovarian Carcinomas</p> <p>23 Curriculum Vitae 57</p> <p>24 Benjamin Neel</p> <p>2/22/19</p>

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<p style="text-align: right;">Page 10</p> <p>1 - - -</p> <p>2 DEPOSITION SUPPORT INDEX</p> <p>3 - - -</p> <p>4</p> <p>5 Direction to Witness Not to Answer</p> <p>6 PAGE LINE</p> <p>7 None.</p> <p>8 Request for Production of Documents</p> <p>9 PAGE LINE</p> <p>10 None.</p> <p>11 Stipulations</p> <p>12 PAGE LINE</p> <p>13 None.</p> <p>14 Questions Marked</p> <p>15 PAGE LINE</p> <p>16 None.</p> <p>17</p> <p>18</p> <p>19</p> <p>20</p> <p>21</p> <p>22</p> <p>23</p> <p>24</p>	<p style="text-align: right;">Page 12</p> <p>1 EXAMINATION</p> <p>2 - - -</p> <p>3 BY DR. THOMPSON:</p> <p>4 Q. Good morning, Dr. Neel.</p> <p>5 A. Good morning.</p> <p>6 Q. My name is Margaret</p> <p>7 Thompson, and I'll be taking your</p> <p>8 deposition today. Have you ever had your</p> <p>9 deposition taken before?</p> <p>10 A. Yes.</p> <p>11 Q. What were the circumstances?</p> <p>12 A. In a -- in a case, the</p> <p>13 so-called Potti-Nevins case. I gave a</p> <p>14 deposition for -- in the -- for the</p> <p>15 defendant. It was a matter involving</p> <p>16 scientific fraud at Duke University.</p> <p>17 Q. Oh. That's my alma mater.</p> <p>18 A. And I also was deposed in a</p> <p>19 malpractice suit when I was a resident in</p> <p>20 Boston.</p> <p>21 Q. As a defendant?</p> <p>22 A. As a defendant.</p> <p>23 Q. And are those the only two</p> <p>24 times --</p>
<p style="text-align: right;">Page 11</p> <p>1 - - -</p> <p>2 THE VIDEOGRAPHER: We are</p> <p>3 now on the record. My name is</p> <p>4 Henry Marte. I'm a videographer</p> <p>5 with Golkow Litigation Services.</p> <p>6 Today's date is March 19,</p> <p>7 2019, and the time is 8:56 a.m.</p> <p>8 This videotaped deposition</p> <p>9 is being held at Four Times</p> <p>10 Square, New York, New York, in the</p> <p>11 matter of Talcum Powder</p> <p>12 Litigation.</p> <p>13 The deponent today is Dr.</p> <p>14 Benjamin Neel.</p> <p>15 All appearances are noted on</p> <p>16 the stenographic record.</p> <p>17 Will the court reporter</p> <p>18 please administer the oath to the</p> <p>19 witness.</p> <p>20 - - -</p> <p>21 ... BENJAMIN G. NEEL, M.D., Ph.D.,</p> <p>22 having been first duly sworn, was</p> <p>23 examined and testified as follows:</p> <p>24 - - -</p>	<p style="text-align: right;">Page 13</p> <p>1 A. Yes.</p> <p>2 Q. -- that you've had your</p> <p>3 deposition taken?</p> <p>4 And I assume the scientific</p> <p>5 fraud case was at least over four years</p> <p>6 ago, right?</p> <p>7 A. It was a little over four</p> <p>8 years ago, right before the -- the</p> <p>9 deposition was taken right before I</p> <p>10 started at NYU Langone, which was</p> <p>11 January 2015. So the deposition was</p> <p>12 taken in October of 2014, so Columbus Day</p> <p>13 weekend.</p> <p>14 Q. Okay. And you're aware that</p> <p>15 the purpose of today is for me to gain a</p> <p>16 thorough understanding of your opinions</p> <p>17 and the basis for those opinions?</p> <p>18 A. Yes.</p> <p>19 Q. Your report states that your</p> <p>20 opinions are given to a reasonable degree</p> <p>21 of scientific certainty.</p> <p>22 What does that mean to you?</p> <p>23 A. It means that I've</p> <p>24 considered all of the papers and also</p>

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<p style="text-align: right;">Page 14</p> <p>1 additional information that is contained 2 in my report. And based on my more than 3 30 years of scientific credentials and 4 experience in the cancer biology and 5 cellular molecular biology field, that I 6 have offered my opinion based on that 7 criteria, those criteria. 8 Q. And how confident do you 9 have to be in your opinions to be able to 10 claim that it's a reasonable degree? 11 A. I'm quite confident in my 12 opinions on this matter based on my 13 30 years of experience. 14 Q. Would that be 100 percent? 15 A. I'm 100 percent -- I 16 wouldn't write it if I wasn't 100 percent 17 confident in my opinions. 18 Q. And Dr. Neel, you are a 19 medical doctor as well as a Ph.D. 20 researcher, correct? 21 A. That's correct. 22 Q. Do you currently see 23 patients? 24 A. No.</p>	<p style="text-align: right;">Page 16</p> <p>1 A. Yes. 2 Q. -- as well? 3 So let me just review some 4 of the ground rules today to remind you. 5 If you don't understand a question, 6 please let me know so I can hopefully put 7 it in a form where you do understand. 8 Okay? 9 A. Okay. 10 Q. And I'll do my best to let 11 you finish your answer, and probably best 12 for you to let me finish my question too, 13 for lots of reasons, but primarily so our 14 court reporter can get both of our 15 statements down without any problems. 16 Okay? 17 A. Sure. 18 Q. And if you need a break, 19 just let me know -- 20 A. Okay. 21 Q. -- and we'll take one. 22 I've marked Exhibit 1 as a 23 notice of deposition. 24 (Document marked for</p>
<p style="text-align: right;">Page 15</p> <p>1 Q. When did you last have a 2 clinical practice? 3 A. 19 -- well I never had a 4 private practice or an individual 5 practice. I stopped seeing patients when 6 I began my faculty position at Harvard 7 Medical School in 1988. 8 Q. After residency? 9 A. Yes. 10 Q. In internal medicine? 11 A. Yes. 12 Q. And do you currently 13 diagnose ovarian cancer in women? 14 A. No. 15 Q. Do you treat women with 16 ovarian cancer? 17 A. No. 18 Q. Have you ever treated women 19 with ovarian cancer? 20 A. Only in the context of my 21 health staff training. 22 Q. Okay. And would that be the 23 last time that you performed a pelvic 24 exam --</p>	<p style="text-align: right;">Page 17</p> <p>1 identification as Exhibit 2 Neel-1.) 3 BY DR. THOMPSON: 4 Q. Have you seen this document, 5 Dr. Neel? 6 A. Yes. 7 Q. When did you see it? 8 A. Yesterday. 9 Q. And I understand that 10 objections have been filed. But -- and 11 did you bring anything with you today in 12 response to this notice of deposition? 13 A. No. 14 Q. For example, Number 3 says a 15 copy of your complete file or files. Do 16 you have a file related to the talcum 17 powder litigation? 18 A. Only insofar as I collect 19 the papers for my report, yes. 20 Q. How do you collect those? 21 A. On my computer. 22 Q. Do you have a certain 23 location where you maintain those files? 24 A. Yes.</p>

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<p>1 Q. And do you have any notes or 2 highlights on the articles? 3 A. On the articles, no. 4 Q. Any notes or -- in the file 5 where you keep your articles? 6 A. Only insofar as I, you know, 7 was preparing my report. There's some 8 notes about the text that I'm going to 9 use in my report. 10 Q. Okay. I also have marked a 11 copy of your expert report. 12 (Document marked for 13 identification as Exhibit 14 Neel-2.) 15 BY DR. THOMPSON: 16 Q. Is this the report that you 17 were referring to that -- 18 A. Yes. 19 Q. -- you kept drafts on your 20 computer? 21 A. Yes. 22 MS. SHARKO: For the record, 23 this is Exhibit 2? 24 DR. THOMPSON: This is</p>	<p>1 the references that are cited by -- in 2 numerical order in the report. 3 Q. And I'm also marking 4 Exhibit 3, which is an -- additional 5 references that -- it's titled "Materials 6 Considered." 7 And what is the list of 8 materials considered? 9 A. I'm a little confused by 10 your question. It says what they are. 11 Q. How does that differ from 12 the references that are attached to your 13 expert report? 14 A. Oh well, if I cited 15 something directly in the report, it's in 16 the references. If there were things 17 that I was given or that I looked 18 through, that's on materials considered. 19 Q. Were you -- were you given 20 the references on the materials 21 considered by counsel? 22 A. A subset of the materials 23 were sent to me at the beginning. I made 24 several other searches of my own and</p>
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<p>1 Exhibit 2. 2 MS. SHARKO: Shall we be 3 calling these Neel-1 and 2? 4 MS. O'DELL: I think 5 Michelle will write that in 6 afterwards. 7 BY DR. THOMPSON: 8 Q. And we'll come back, of 9 course, to that report throughout the 10 day. So feel free to keep that close by 11 if you'd like to. 12 (Document marked for 13 identification as Exhibit 14 Neel-3.) 15 BY DR. THOMPSON: 16 Q. And I've marked as Exhibit 3 17 the -- and you say that attached to your 18 report are the references that you 19 listed. And are those references that 20 are actually cited or referred to in the 21 report itself? 22 A. Can I -- may I look? 23 Q. Yes, please. 24 A. Yes. These references are</p>	<p>1 downloaded those papers. And some of the 2 papers I was unable to easily access from 3 my remote location. And I asked the 4 lawyers to have them sent to me. So some 5 of them I got that way. 6 Q. Would you be able to 7 identify which you found yourself and 8 which you were provided to by the 9 lawyers? 10 A. Not easily. I mean, I went 11 through and I spent many hours doing 12 this. So I'm not sure. Over time, that 13 blurs a little. 14 Q. And I assume that the expert 15 reports and deposition transcripts were 16 provided to you, correct? 17 A. Yes. 18 Q. When was -- when were you 19 first contacted by lawyers representing 20 Johnson & Johnson about serving as an 21 expert? 22 A. In May of 2017 I believe. 23 Q. And who contacted you? 24 A. John Winter.</p>

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<p style="text-align: right;">Page 22</p> <p>1 Q. And what did Mr. Winter ask 2 you to do? 3 A. He asked me if I would be 4 interested in considering being an expert 5 witness in the talc litigation. 6 Q. And what did you agree to do 7 at that time? 8 A. I agreed to look at the 9 materials that he gave me and make a 10 decision subsequently. 11 Q. Were you asked at that time 12 to offer any criticisms of any 13 plaintiffs' experts? 14 MS. SHARKO: Well, I'm 15 going -- I'm going to object at 16 this point. Isn't this privileged 17 conversations between counsel and 18 the witness? 19 DR. THOMPSON: I believe 20 what he was asked to do at the 21 initiation is fair. 22 MS. SHARKO: I think that's 23 privileged conversations between 24 the lawyer and the witness.</p>	<p style="text-align: right;">Page 24</p> <p>1 misunderstood. 2 Did he -- was any of that 3 material that he asked you to look at, 4 did that include defense -- plaintiff 5 expert reports? 6 A. At the -- the initial batch 7 of materials that I -- that I got had no 8 expert reports from anyone in it. 9 Q. Okay. Were you asked to do 10 any experiments? 11 A. No. 12 Q. Did you offer to do any 13 experiments? 14 A. No. I wouldn't be allowed. 15 Q. Why is that? 16 A. Because it would be a 17 conflict of interest violation of my 18 institution. 19 Q. What is your institution's 20 conflict of interest policy? 21 A. Well, I mean, that's a 22 pretty broad question. Do you want to 23 maybe -- I mean, my conflict -- we have a 24 very long policy which I have not</p>
<p style="text-align: right;">Page 23</p> <p>1 DR. THOMPSON: Okay. All 2 right. 3 MS. SHARKO: You can ask -- 4 you can ask him what he did. I 5 don't think you can ask him about 6 discussions between the lawyer and 7 the witness. 8 BY DR. THOMPSON: 9 Q. In that initial evaluation 10 that you performed to look, did that 11 include evaluating any expert reports 12 from plaintiffs? 13 A. The initial -- are you 14 talking about the initial meeting with 15 Mr. Winter? 16 Q. Well, you -- you said that 17 Mr. Winter furnished you with some 18 literature to review, correct? 19 A. No. I think I said -- maybe 20 I misspoke. But I believe I said that 21 Mr. Winter asked me if I would be willing 22 to look at some material, and I said yes 23 at our initial meeting. 24 Q. Okay. I may have</p>	<p style="text-align: right;">Page 25</p> <p>1 committed to memory. 2 Q. Okay. Did -- have you 3 disclosed to your institution that you're 4 serving as an expert for Johnson & 5 Johnson? 6 A. Yes. 7 Q. And what details did you 8 have to provide regarding that? 9 A. Just the name of the law 10 firm that I was working with. I don't 11 remember the name of Mr. Winter's law 12 firm. Because I recently revised the 13 disclosure because I'm working mostly 14 with Ms. Sharko now which is a different 15 firm. 16 Q. And why would your 17 institution prevent you from doing any 18 experiments? 19 A. I -- I can't comment on 20 the -- 21 MS. SHARKO: Object to the 22 form. 23 THE WITNESS: I can't 24 comment on the basis of the</p>

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<p style="text-align: right;">Page 26</p> <p>1 conflict of interest policy. I 2 can only tell you what it is. 3 BY DR. THOMPSON: 4 Q. And what aspect or what 5 language in that policy has led you to 6 believe that you would be unable to do 7 any experiments? 8 A. Because, for any kind of -- 9 we're not allowed to take financial 10 remuneration from anyone and at the same 11 time do laboratory experiments on the 12 topic. That's considered a conflict of 13 interest as I understand the conflict of 14 interest policy. 15 Q. So what -- what entities 16 would that include? 17 MS. SHARKO: Object to the 18 form. 19 BY DR. THOMPSON: 20 Q. Pharmaceutical companies? 21 A. Yes. If I -- if I get 22 funding -- if I get compensation, private 23 compensation from a pharmaceutical 24 company, or if I own equity in a</p>	<p style="text-align: right;">Page 28</p> <p>1 or any compensation from the company. It 2 was not -- it was just laboratory 3 funding. 4 When I was at Harvard 5 Medical School, I believe in the third -- 6 no, it would have been more like the 7 fourth or fifth year that I was a faculty 8 member, I had a grant from Roche 9 Pharmaceuticals. That was a two-year 10 grant, and it was a competitive grant 11 where Harvard had a -- Harvard, I think 12 it was the department of biochemistry -- 13 one of the departments that I was 14 affiliated with at Harvard, had a -- a 15 relationship with Roche where you could 16 submit competitive grants and then they 17 were reviewed by a group that included 18 Harvard faculty and Roche faculty. And 19 they chose the ones they were interested 20 in. And then so I believe it was a 21 \$75,000 grant that I got for two years. 22 Q. Okay. And -- 23 A. And that was on SHIP1, which 24 I'm also an expert in. I identified both</p>
<p style="text-align: right;">Page 27</p> <p>1 pharmaceutical company or founders 2 equity, I can't do experiments in my 3 laboratory. That's considered to be a 4 conflict of interest at our institution. 5 And most reputable institutions that I 6 have experience with, and Canada. 7 Q. So you receive only public 8 funding in your lab? 9 A. I have -- at the present 10 time? At the present time all of my 11 funding is public or startup funding for 12 my institution. 13 Q. How about at any time? 14 A. When I was at Princess 15 Margaret Cancer Centre in Toronto, which 16 was my second job, I received a -- a 17 grant from Novartis Pharmaceuticals to do 18 studies related to the possible uses of 19 SHIP2 inhibitors, which I'm an expert in, 20 in cancer. So that was a two-year grant 21 that had specific aims and milestones and 22 reports that I had. And it was more like 23 a pharmaceutical funding grant, but I was 24 not receiving any equity in the company</p>	<p style="text-align: right;">Page 29</p> <p>1 of those molecules. 2 Q. Okay. And that -- and that 3 policy goes for lab funding as well as 4 compensation, correct? 5 A. Which policy? 6 Q. The policy that would be 7 conflict of interest that prohibits you 8 from doing any experiments for 9 remuneration. 10 A. No. The conflict of 11 interest policy is that I can't receive 12 personal compensation. We are allowed to 13 receive some -- we are allowed to 14 pursue 20 -- we're allowed to use 15 20 percent of our time outside of -- of 16 our hospital or medical school time for 17 consulting, expert witnesses, 18 participation in biotechnology companies. 19 That money has to be separate from your 20 lab money. 21 Q. Okay. But there would be 22 nothing that would prevent Johnson & 23 Johnson from providing laboratory funding 24 for -- for research or experiments?</p>

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<p style="text-align: right;">Page 30</p> <p>1 A. There would, if I were 2 receiving compensation, as I am for 3 serving as an expert witness in this 4 case. That would be a conflict in my -- 5 my view of the conflict of interest 6 policy. I didn't consult the -- the 7 hospital about that. 8 Q. Okay. And does that same 9 policy apply to anyone in your lab? 10 A. Yes. 11 Q. What did you know about 12 talcum powder and ovarian cancer before 13 you were approached by Mr. Winter? 14 A. I had seen reports in the 15 process of litigation and, you know, 16 that's pretty much it. 17 Q. And you had not reviewed any 18 of the literature regarding the issue, 19 correct? 20 A. That's correct. 21 Q. Did you have any opinions 22 formed at that time? 23 A. No. 24 Q. May I assume that all of the</p>	<p style="text-align: right;">Page 32</p> <p>1 literature to cite? 2 A. Yes. 3 Q. And did you choose the 4 quotes that you include in your report? 5 A. Yes. 6 Q. The references that you 7 cited that are attached to your report, 8 may I assume that those are the ones that 9 you deemed most important relating to 10 your opinions? 11 A. Yes. 12 Q. Did you perform any 13 searches? 14 A. Yes. As I said earlier, I 15 did several searches. 16 Q. What terms did you use? 17 A. Well, I can't remember all 18 of them in detail, but certainly talc and 19 inflammation. Talc and ovarian cancer. 20 I don't remember all of them. But those 21 are a couple. 22 Q. And what's your favorite 23 search engine or site? 24 A. I use both Google and PubMed</p>
<p style="text-align: right;">Page 31</p> <p>1 opinions that you plan to give today are 2 contained in your expert report? 3 MS. SHARKO: Object to the 4 form of the question. It depends 5 what you ask him. 6 THE WITNESS: Should I 7 answer? 8 MS. SHARKO: Yes, you can 9 answer. 10 THE WITNESS: How could I 11 say that until I hear what you ask 12 me? I can't answer that. 13 BY DR. THOMPSON: 14 Q. Or additional opinions that 15 you give in response to my questions. 16 Would that be fair? 17 A. Yes. 18 Q. Who wrote your expert 19 report? 20 A. I did. 21 Q. Did you write every word of 22 the expert report? 23 A. Yes. 24 Q. Did you choose the</p>	<p style="text-align: right;">Page 33</p> <p>1 for different searches. I find them -- 2 they provide different information. 3 Q. The -- on the materials 4 considered, Exhibit Number 3, there are a 5 bunch of plaintiff expert reports listed. 6 Did you read all of those? 7 A. No. 8 Q. Can you go through and tell 9 me which ones you did read? 10 A. I read Dr. Saed's report. I 11 read Dr. Zelikoff's report. And I read 12 Dr. Smith-Bindman's report, and I read is 13 it Dr. -- is it Levy or Levy's report? 14 I'm not sure how to pronounce his name. 15 I'm sorry. 16 Q. Any others? 17 A. No. 18 Q. You did not look at 19 Dr. Crowley's report? 20 A. No. 21 Q. Why not? 22 A. I just didn't think it 23 relevant. 24 Q. Do you know what</p>

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<p style="text-align: right;">Page 34</p> <p>1 Dr. Crowley's report addressed? 2 A. I don't recall. I scanned 3 through the intros of all of them. But I 4 didn't think it was really relevant. 5 Q. Dr. Crowley's report 6 addressed the fragrance chemicals in 7 Johnson's Baby Powder. Was that not 8 relevant for you? 9 A. No, not in my opinion. 10 Q. And why is that? 11 A. Because that wasn't the 12 issue that I was asked to address. I was 13 asked to address Johnson & Johnson Baby 14 Powder studies that used the Baby Powder. 15 So what was in them was irrelevant to the 16 conclusion. It was just the conclusion, 17 the effects that were relevant. And I 18 was asked to address the issue of talc 19 and ovarian cancer. 20 Q. So it doesn't matter to you 21 what else is in the Baby Powder? 22 A. Not from the standpoint of 23 experiments that involve the Baby Powder. 24 It's just the results of the Baby Powder.</p>	<p style="text-align: right;">Page 36</p> <p>1 are talking about today, correct? 2 A. I don't know. That's -- I 3 mean, I considered them for sure. 4 Q. Okay. When you say talc are 5 you referring to talcum powder? 6 A. Yes. 7 Q. Are you referring to talcum 8 powder that's platy? 9 A. I'm referring to the talcum 10 powder that was used in the 11 epidemiological studies and in the 12 experiments of Dr. Saed and others that I 13 considered for the purposes of my report. 14 I can't give you an exhaustive listing of 15 what they use. But I did consider those 16 papers in issuing my opinion. 17 Q. Well, those are two 18 different things. The epidemiology 19 studies are typically done calling the 20 agent that's being asked about talcum 21 powder. And Dr. Saed's experiments were 22 specifically done with Johnson's Baby 23 Powder, correct? 24 MS. SHARKO: Object to the</p>
<p style="text-align: right;">Page 35</p> <p>1 Q. And throughout your report 2 you refer to talc. What do you mean by 3 that? 4 A. I mean talc. What do you 5 mean by that? 6 Q. Well, is it Baby Powder or 7 is it talc? 8 A. No -- well, it's -- the talc 9 that I referred to is generic talc. It 10 could be talc from chemical companies. 11 Whatever was used in the experiments in 12 the reports that -- and/or the studies 13 that I read that were epidemiological 14 based. 15 Q. What are the products that 16 are at issue today in the litigation? 17 A. I'm not an expert on what's 18 involved in litigation. I know that 19 Johnson & Johnson Baby Powder and Baby 20 Shower (sic) are involved in the 21 litigation. I'm not aware of any other 22 specific products that are involved. 23 Q. So Johnson Baby Powder and 24 Shower to Shower are the products that we</p>	<p style="text-align: right;">Page 37</p> <p>1 form of the question. Lacks 2 foundation. 3 THE WITNESS: The 4 epidemiological studies, in fact, 5 were performed using a variety of 6 different products. So there 7 wasn't a single product used. But 8 Johnson & Johnson products were in 9 some of them. Some of the studies 10 also included cornstarch. 11 The Saed studies, as I 12 recall, but we have to look at 13 them in detail to be sure, 14 included talc from chemical 15 companies and Johnson & Johnson 16 products. 17 BY DR. THOMPSON: 18 Q. And we will get to 19 Dr. Saed's work. Did you see the paper 20 that Dr. Saed just published in the last 21 few weeks? 22 A. I didn't see the final 23 version of the paper. But I saw the 24 accepted version that was supplied to us</p>

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<p>1 after his deposition. And I reviewed 2 that. 3 Q. Why did you not look at the 4 final published paper? 5 A. Because the -- as far as I 6 know, the paper was accepted. So an 7 accepted paper is the same as the 8 published paper. But I'm happy to look 9 at it if you'd like. 10 Q. I'm just asking you why you 11 didn't think that was important to look 12 at yourself. 13 A. Because -- 14 MS. SHARKO: Object to the 15 form of the question. 16 THE WITNESS: Because an 17 accepted paper, in my experience, 18 is identical to the actual paper 19 except for minor editorial, you 20 know, placements of figures and 21 things like that. Once it's 22 accepted, it's not changed. 23 BY DR. THOMPSON: 24 Q. So your opinion is that in</p>	<p>1 which talcum powder may cause or 2 contribute to ovarian cancer, doesn't it 3 make a difference what the components of 4 that talcum powder are? 5 A. No. If I am referring to 6 the papers that are published by experts 7 for the plaintiffs to argue for a 8 pathogenic role, I should be considering 9 what they use. That's the only role of 10 an issue here in my opinion. 11 Q. So if it's shown that talcum 12 powder contains fibrous talc, which is 13 listed as a Group 1 carcinogen by IARC, 14 that would not matter to you in your 15 opinions as to what the mechanism might 16 be for the carcinogenesis of Baby 17 Powder -- 18 MS. SHARKO: Object to 19 the from of the -- 20 BY DR. THOMPSON: 21 Q. -- correct? 22 MS. SHARKO: Object to the 23 form of the question. Lacks 24 foundation.</p>
Page 39	Page 41
<p>1 the final accepted paper, there was a 2 discussion of talcum powder other than 3 Johnson's Baby Powder; is that right? 4 A. I don't recall. I'm happy 5 to look at the paper. 6 Q. We'll look at that a little 7 bit later. 8 And does talcum powder 9 include fibrous talc? 10 A. Talcum powder includes what 11 I just said. It's whatever was in the 12 products that were used in the 13 epidemiology studies and whatever was 14 used in any of the individual papers. 15 And I'm happy to go through any single 16 one of them with you and review the 17 details. But I obviously can't remember 18 which products were used in every single 19 epidemiology study that I reviewed and in 20 every single paper that I reviewed, 21 including, you know, papers from Dr. Saed 22 and others. 23 Q. From a molecular standpoint, 24 here to testify about the mechanism by</p>	<p>1 THE WITNESS: Can you repeat 2 the question, please? 3 BY DR. THOMPSON: 4 Q. So if it's shown that talcum 5 powder contains fibrous talc, which is 6 listed as a Group 1 carcinogen by IARC, 7 that would not matter to you in your 8 opinions as to what the mechanism might 9 be, correct? 10 A. Yes. That's correct. 11 Because my opinion is based on the 12 studies that involved the application of 13 talc, including Johnson & Johnson 14 products, perineally, and also in some 15 cases injected and applied to cells. And 16 that would -- if, you know, the products 17 have any substance in them, then they 18 should have revealed a carcinogenic 19 effect in those studies or they should 20 have revealed something supporting the 21 plaintiffs' experts arguments. But I 22 found no evidence that that's the case. 23 None. 24 Q. Are you speaking of</p>

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<p>1 epidemiological evidence?</p> <p>2 A. I'm speaking of every -- of</p> <p>3 all of the evidence that I covered in my</p> <p>4 report. And I'm happy to go through any</p> <p>5 individual one. But it's all of the</p> <p>6 evidence that I considered in my report.</p> <p>7 I found no compelling scientific evidence</p> <p>8 to support the position that talc causes</p> <p>9 ovarian cancer.</p> <p>10 Q. Okay. We'll get to that a</p> <p>11 little bit more later.</p> <p>12 And you did not look at</p> <p>13 Dr. Longo's reports, correct?</p> <p>14 A. That's correct.</p> <p>15 Q. And for the same reason that</p> <p>16 you did not consider it relevant to your</p> <p>17 opinions?</p> <p>18 A. Correct.</p> <p>19 Q. And do you know what</p> <p>20 Dr. Longo's report addressed?</p> <p>21 A. I don't recall. As I told</p> <p>22 you I scanned through each of them to</p> <p>23 decide which ones I should look at in</p> <p>24 more detail.</p>	<p>1 Q. Do you know who Dr. David</p> <p>2 Kessler is?</p> <p>3 A. I don't recall.</p> <p>4 Q. And you have listed</p> <p>5 references to various websites. What was</p> <p>6 the purpose for selecting these websites</p> <p>7 to include on your materials considered?</p> <p>8 A. Well, there were different</p> <p>9 purposes for different websites. Do you</p> <p>10 want to walk through them one by one?</p> <p>11 Q. No, we'll get back to some</p> <p>12 of them I think.</p> <p>13 Did you list any websites</p> <p>14 that did identify a risk of ovarian</p> <p>15 cancer with the perineal use of talcum</p> <p>16 powder products?</p> <p>17 A. I don't recall what's in</p> <p>18 every one of the websites, but I don't</p> <p>19 believe so.</p> <p>20 Q. You are aware that there are</p> <p>21 websites that would list talcum powder</p> <p>22 use as a risk factor for ovarian cancer,</p> <p>23 correct?</p> <p>24 A. I'm not aware of what</p>
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<p>1 Q. So you were not aware that</p> <p>2 Dr. Longo actually tested a number of</p> <p>3 Baby Powder and Shower to Shower samples</p> <p>4 from Johnson & Johnson over decades when</p> <p>5 they were produced, correct?</p> <p>6 A. Correct.</p> <p>7 MS. SHARKO: Object to the</p> <p>8 form of the question.</p> <p>9 BY DR. THOMPSON:</p> <p>10 Q. And you did not look at any</p> <p>11 of the GYN oncology reports, correct?</p> <p>12 That would be Dr. Daniel</p> <p>13 Clarke-Pearson, Dr. Ellen Blair Smith or</p> <p>14 Dr. Judy Wolf?</p> <p>15 A. That's correct. I -- I</p> <p>16 looked through them -- I looked at the --</p> <p>17 at the general, you know, statements in</p> <p>18 the beginning and decided they weren't</p> <p>19 really relevant to my expertise.</p> <p>20 Therefore, I didn't look at them in</p> <p>21 detail.</p> <p>22 Q. Did you read the expert</p> <p>23 report of Dr. David Kessler?</p> <p>24 A. No.</p>	<p>1 websites that I didn't look at say. I'm</p> <p>2 aware of what websites that I did look at</p> <p>3 say.</p> <p>4 Q. So you did not see any</p> <p>5 websites that listed talcum powder use as</p> <p>6 a risk factor; is that correct?</p> <p>7 Or you don't know one way or</p> <p>8 the other?</p> <p>9 A. I don't recall if I did or I</p> <p>10 didn't.</p> <p>11 Q. And you reviewed IARC 2010,</p> <p>12 correct?</p> <p>13 A. Correct.</p> <p>14 Q. And what is IARC?</p> <p>15 A. International Agency For</p> <p>16 Research and Cancer, I believe.</p> <p>17 Q. And what is the subject</p> <p>18 matter of the monograph from 2010?</p> <p>19 A. It covers several things. I</p> <p>20 don't remember the exact details, but</p> <p>21 we -- I can look it up.</p> <p>22 Q. We'll come back to it.</p> <p>23 And is it your understanding</p> <p>24 that the IARC 2010 monograph reviewed</p>

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<p style="text-align: right;">Page 46</p> <p>1 literature as of 2006, correct?</p> <p>2 A. I can't recall in detail</p> <p>3 when they cut off the literature.</p> <p>4 Q. We'll look at that.</p> <p>5 And you are aware that the</p> <p>6 IARC monograph in 2010, published,</p> <p>7 reviewing literature up to 2006,</p> <p>8 specifically dealt with non-asbestiform</p> <p>9 talc, correct?</p> <p>10 A. That's my recollection. But</p> <p>11 again, I read that a while ago. And I'm</p> <p>12 happy to go back and look at it with you</p> <p>13 if you want to jog my memory.</p> <p>14 Q. That's a pretty important</p> <p>15 fact, don't you think?</p> <p>16 A. It's not material to the</p> <p>17 question at hand as far as I can tell.</p> <p>18 Because as, again, I was asked to review</p> <p>19 the issue of, you know, Johnson & Johnson</p> <p>20 products and/or talc and ovarian cancer</p> <p>21 with respect to the evidence in the</p> <p>22 scientific literature as to its</p> <p>23 carcinogenicity, and that's what I</p> <p>24 reviewed. And whatever talc was used in</p>	<p style="text-align: right;">Page 48</p> <p>1 suppliers like -- chemical suppliers like</p> <p>2 Sigma.</p> <p>3 And each study is different.</p> <p>4 But the -- the studies that I cited in my</p> <p>5 report all used various forms of "talc"</p> <p>6 and that's what I considered in offering</p> <p>7 my opinion.</p> <p>8 Q. You'll agree that the</p> <p>9 molecular studies identified where the</p> <p>10 talc came from or the talcum powder came</p> <p>11 from, correct?</p> <p>12 A. Yes.</p> <p>13 Q. The epidemiological studies</p> <p>14 typically do not, correct?</p> <p>15 A. I don't believe that that is</p> <p>16 correct. Some of them say specifically</p> <p>17 what products they are. And some of them</p> <p>18 are not as specific. So it's not a</p> <p>19 one-size-fits-all for that question.</p> <p>20 Q. Are you aware of an</p> <p>21 epidemiological study that actually</p> <p>22 refers to what actual product was used by</p> <p>23 the women included in the study?</p> <p>24 A. My recollection is several</p>
<p style="text-align: right;">Page 47</p> <p>1 those studies would have, you know, been</p> <p>2 the relevant talc. So that's what I</p> <p>3 reviewed.</p> <p>4 Q. So studies that were --</p> <p>5 would address asbestos and ovarian cancer</p> <p>6 are not relevant?</p> <p>7 A. Not insofar as I can tell.</p> <p>8 Because I was looking at the issue of</p> <p>9 Johnson & Johnson products and/or talc as</p> <p>10 defined by the authors of the papers that</p> <p>11 used these materials, and/or the authors</p> <p>12 of the epidemiological studies that</p> <p>13 studied this issue on -- in offering my</p> <p>14 opinion.</p> <p>15 Q. And you are talking about</p> <p>16 the epidemiological studies, correct?</p> <p>17 A. No. I'm talking about the</p> <p>18 epidemiological studies which used</p> <p>19 certain things. And then I'm talking</p> <p>20 about the bio -- biological studies such</p> <p>21 as they are, that used various forms of</p> <p>22 talc, whether it's Johnson -- in some</p> <p>23 case it's Johnson & Johnson products</p> <p>24 directly. In other cases, talc from</p>	<p style="text-align: right;">Page 49</p> <p>1 said Johnson & Johnson's products. But</p> <p>2 we'd have to go through all of the</p> <p>3 24-case-control studies and three cohort</p> <p>4 studies that I looked at.</p> <p>5 Q. Do you know what Johnson &</p> <p>6 Johnson's market share of Baby Powder has</p> <p>7 been over the years?</p> <p>8 A. I have no idea.</p> <p>9 Q. You also reviewed the IARC</p> <p>10 monograph in 2012, correct?</p> <p>11 A. Which one is that?</p> <p>12 Q. That's the one related to</p> <p>13 asbestos.</p> <p>14 A. I looked at that very</p> <p>15 cursorily. I really didn't have the time</p> <p>16 to do an exhaustive study of asbestos and</p> <p>17 ovarian cancer. I looked at it</p> <p>18 cursorily. And several other papers.</p> <p>19 Q. And even if Johnson &</p> <p>20 Johnson's Baby Powder and Shower to</p> <p>21 Shower have -- are shown to contain</p> <p>22 asbestos, that was -- reviewing that</p> <p>23 evidence and that data were not</p> <p>24 important?</p>

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<p>1 A. No, because the issue is 2 whether there is any compelling 3 scientific evidence that Johnson & 4 Johnson's products, when applied 5 perineally, give rise to an increased 6 incidence of ovarian cancer, and/or 7 whether there was any evidence that 8 Johnson & Johnson products, when applied 9 in experimental animals have any evidence 10 of causing pre or neoplastic conditions 11 of the ovaries or fallopian tubes. 12 That was the issue that I 13 considered in issuing my report. And 14 therefore, the issue is what's -- what 15 the Johnson & Johnson products do, not 16 whether asbestos is involved in ovarian 17 cancer. 18 Q. Are you aware of animal 19 studies that use Johnson & Johnson Baby 20 Powder? 21 A. I would have to go back and 22 look at the actual studies to see what 23 was used in those studies. 24 Q. You don't know that?</p>	<p>1 But I didn't have a chance to study it in 2 any detail. 3 Q. You didn't ask -- 4 A. In any event, it's a draft, 5 so it hasn't been, you know, finalized. 6 So I don't really think it's relevant 7 until it's finalized. 8 Q. Well, do you know anything 9 about the policy that Health Canada 10 follows to publish a draft to open up for 11 comments -- 12 A. No. 13 Q. -- before it's finalized? 14 A. No. 15 Q. Did you review the 16 conclusions of the Health Canada risk 17 assessment draft that you were provided 18 yesterday? 19 A. Not in -- I didn't have time 20 really to review it in any significant 21 detail. So the answer to that is no. 22 But I'm happy to do it now. 23 Q. Well, you know you referred 24 to the Health Canada risk assessment</p>
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<p>1 A. I don't remember. 2 Q. That wasn't something that 3 would have been important? 4 A. I read through all of the 5 animal studies, none of which show any 6 significant carcinogenic effect of talc 7 that was used in the studies. 8 Q. We'll get to those. 9 You reviewed the Health 10 Canada risk assessment, correct? 11 A. Are we talking about the 12 Taher, et al., paper? 13 Q. No, we are talking about the 14 risk assessment published by -- draft 15 published by Health Canada. 16 A. I haven't actually read the 17 draft. 18 Q. Why not? 19 A. I haven't seen it. 20 Q. So you were not provided the 21 Health Canada risk assessment? 22 A. I was given -- you know, 23 yesterday, you know, the lawyers showed 24 me briefly there was a health assessment.</p>	<p>1 draft in your report? 2 A. No, not that I recall. 3 Where do I refer -- I refer to the Taher, 4 et al., paper which was the basis for the 5 study that was being done at Health 6 Canada. 7 Q. How do you know that the 8 Taher paper was the basis for the Health 9 Canada risk assessment? 10 A. I think it says it in the 11 paper. 12 Q. Okay. We'll get to that 13 when we get to that section. 14 And you reviewed an FDA 15 letter in response to a citizen's 16 petition, correct? 17 A. Yes. 18 Q. And was that provided to you 19 by counsel? 20 A. Yes. 21 (Document marked for 22 identification as Exhibit 23 Neel-4.) 24 BY DR. THOMPSON:</p>

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<p>1 Q. I've marked as Exhibit 4 2 Appendix A to your report. And just tell 3 me what this is. 4 A. This is a list -- 5 MS. SHARKO: Just take your 6 time and look through it. 7 THE WITNESS: This is a list 8 of the most recent genome-wide 9 association studies. That show 10 genome-wide association -- that 11 show association with specific 12 single-nucleotide polymorphisms 13 with increased risk of ovarian 14 cancer. 15 BY DR. THOMPSON: 16 Q. And how does something make 17 it to the -- this list? 18 A. How does it make it to this 19 list? When there's been a -- any 20 publication of a genome-wide association 21 study is aggregated. 22 Q. And so that's when there 23 have been enough studies published on a 24 certain gene to reach statistical</p>	<p>1 THE WITNESS: I wasn't done. 2 BY DR. THOMPSON: 3 Q. Sorry. 4 A. So some of -- you know, the 5 ones that are over 10-8 are the only ones 6 that can be considered as documented risk 7 SNPs. 8 Q. And there are new SNPs being 9 reported all the time. You would agree 10 with that, correct? 11 A. Well, the SNPs aren't being 12 reported. The SNPs have pretty much -- 13 you know, the SNPs that are used in the 14 genome-wide association studies are the 15 SNPs that are on standard panels. 16 What do you mean new SNPs 17 being reported all the time? There are 18 private SNPs between any two individuals. 19 If I sequence you and I sequence me, we 20 might find, you know, a new 21 single-nucleotide polymorphism. But 22 that's a privacy SNP for you or for me. 23 It's not one of the ones that was used to 24 map genes.</p>
Page 55	Page 57
<p>1 significance, correct? 2 A. Yes. Well, the statistical 3 significance of each -- well, there's 4 different levels of statistical 5 significance in the GWAS for every 6 location that's cited in the GWAS. So 7 some of them are -- and if you go on the 8 website and look at it, you'll see that 9 it lists the P-value for every 10 association. 11 So some of them have reached 12 genome-wide significance, and some of 13 them haven't. So the ones that are 14 believed to be documented associations 15 are those that have reached genome-wide 16 significance. And that means that they 17 have less than 10-8. There are other 18 genome-wide association snips that have 19 reached less than 10-8. 20 Q. And there are snips -- 21 MS. SHARKO: Wait, wait, 22 wait. 23 Are you done with your 24 answer?</p>	<p>1 Q. Right. I understand that. 2 But there is ongoing research in this 3 area, correct? 4 A. Yes, there's ongoing 5 research in genetic basis of all cancers. 6 (Document marked for 7 identification as Exhibit 8 Neel-5.) 9 BY DR. THOMPSON: 10 Q. Exhibit 5 is your CV. It 11 appears that that was updated 12 February 22nd, 2019, correct? 13 A. Yes. 14 Q. And you have quite a few 15 publications, I see. 16 A. Not as many as I'd like. 17 Q. Well, you still have a lot 18 of time, right, in your career, I hope. 19 How -- how many of these 20 deal with ovarian cancer? 21 A. I don't know. We can go 22 through each of them. I don't know 23 offhand. 24 Q. Does eight sound about</p>

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<p style="text-align: right;">Page 58</p> <p>1 right?</p> <p>2 A. I can count them. Possibly</p> <p>3 eight. But you know, cancer biology is</p> <p>4 much more broad than a specific cancer.</p> <p>5 So, I mean, my expert opinion is based on</p> <p>6 30 years of research, actually more than</p> <p>7 30. 30 years as a faculty member at</p> <p>8 Harvard Medical School, Princess Margaret</p> <p>9 and now NYU. And before that, you know,</p> <p>10 graduate school and Ph.D. and post-doc --</p> <p>11 Ph.D. and post-doc training. So I've had</p> <p>12 about 36 years of -- no, 39 years of --</p> <p>13 wow, that's a lot of time -- 39 years of</p> <p>14 research experience in this field.</p> <p>15 From the earliest days of</p> <p>16 the cancer biology field, I was involved</p> <p>17 in, you know, some of the earliest major</p> <p>18 discoveries that led to the molecular age</p> <p>19 of cancer.</p> <p>20 Q. And obviously that</p> <p>21 experience with other types of cancer are</p> <p>22 relevant to the study of ovarian cancer</p> <p>23 and the type -- subtypes, correct?</p> <p>24 A. I think so, yes.</p>	<p style="text-align: right;">Page 60</p> <p>1 amplification, certain forms of KRAS</p> <p>2 mutations, certain forms of BRAF</p> <p>3 mutations.</p> <p>4 There's actually drugs in</p> <p>5 the clinic now that are trying to target</p> <p>6 this agent, this -- this molecule.</p> <p>7 It's also mutated in a</p> <p>8 germ -- under a germ-line mutations in a</p> <p>9 disease called Noonan syndrome. And</p> <p>10 we've done a lot of the work on that.</p> <p>11 And there are also different germ-line</p> <p>12 mutations in the disease cause Noonan</p> <p>13 syndrome with multiple lentigines. We've</p> <p>14 done a lot of work on that. We did the</p> <p>15 first mouse models for both of those</p> <p>16 disorders.</p> <p>17 We discovered that there's a</p> <p>18 third type of mutation in SHIP2 or PTPN11</p> <p>19 that causes metachondromatosis, which is</p> <p>20 a rare cancer of the bone. We discovered</p> <p>21 that SHIP2 acts as tumor suppressor gene</p> <p>22 in that.</p> <p>23 So our lab is working a lot</p> <p>24 on using -- on figuring out how to best</p>
<p style="text-align: right;">Page 59</p> <p>1 Q. Are there any articles on</p> <p>2 your CV that relate directly to talcum</p> <p>3 powder and potential carcinogenesis?</p> <p>4 A. No.</p> <p>5 Q. Are there any articles on</p> <p>6 your CV that relate to asbestos?</p> <p>7 A. No.</p> <p>8 Q. Are there any articles on</p> <p>9 your CV that relate to particles of any</p> <p>10 kind?</p> <p>11 A. No.</p> <p>12 Q. Describe for me the</p> <p>13 research -- understanding it's a big lab,</p> <p>14 but generally speaking, what type of</p> <p>15 research is your lab currently doing?</p> <p>16 A. Well, it's divided into</p> <p>17 three main areas. One area has to do</p> <p>18 with SHIP2, which we discussed --</p> <p>19 discovered, which is a critical component</p> <p>20 of growth factor receptor, cytokine</p> <p>21 receptor, and integrin signaling pathways</p> <p>22 and is critical for the transduction of</p> <p>23 signals from activated oncogenes, such as</p> <p>24 the receptor tyrosine kinase</p>	<p style="text-align: right;">Page 61</p> <p>1 deploy SHIP2 inhibitors in the -- in the</p> <p>2 clinic and how to combine them with other</p> <p>3 agents. So that's about a third.</p> <p>4 And then we have a third of</p> <p>5 the lab that's working on ovarian cancer,</p> <p>6 pathogenesis, including studies related</p> <p>7 to the cell of origin, studies related to</p> <p>8 the heterogeneity in ovarian cancer using</p> <p>9 the single cell RNA sequencing, and</p> <p>10 various type of single cell RNA FISH.</p> <p>11 And then we have a fourth --</p> <p>12 sorry, a third part of the lab, which</p> <p>13 is -- oh, I forgot. I'm sorry.</p> <p>14 And then we've also</p> <p>15 developed novel organoid systems for both</p> <p>16 the fallopian tube and the ovarian</p> <p>17 surface epithelium in the mouse. And</p> <p>18 we're using that -- those models to</p> <p>19 engineer in the specific mutations that</p> <p>20 have been found in ovarian -- human</p> <p>21 ovarian cancer so we can develop</p> <p>22 syngeneic mouse models to study how to</p> <p>23 best treat these tumors using</p> <p>24 combinations of targeted agents and</p>

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<p>1 immunotherapy, including platinum PARP 2 inhibitors, trying to figure out how 3 cyclin E tumors can be treated since 4 they're not treated by platinum very 5 well. 6 And then the third area of 7 the lab has to do with another 8 phosphatase that we discovered or that we 9 cloned. We didn't discover it. We were 10 the first to clone it, called PPM1 or 11 PP1B. And we're working on how that's 12 involved in breast cancer pathogenesis 13 by -- and in particular how it 14 regulates -- how -- how knocking down or 15 inhibiting PP1B sensitizes breast cancer 16 cells, or certain types of breast cancer 17 cells, to hypoxia using -- and in 18 particular, how the -- there is an 19 interaction between this PP1B and this 20 novel E3 ligase called RNF213, which is 21 the disease gene for moyamoya syndrome 22 which is a very rare syndrome that causes 23 precocious strokes in children. 24 So that's the -- that's the</p>	<p>1 About 50 of which are genomically 2 characterized, and we are collaborating 3 with people to use those. 4 And we are sometimes 5 making -- we also make organoid -- we're 6 working on organoid systems from humans. 7 So we get tissues from our Winthrop 8 colleagues. And that's under an IRB 9 protocol, so -- but we don't do any 10 clinical trials. 11 I'm consulting on a clinical 12 trial that has to do with a different 13 area of research that we transiently were 14 involved in that's distantly related to 15 the moyamoya syndrome thing. I don't 16 know that you want to go into that, but 17 I'm happy to discuss that. 18 Q. Probably not. 19 A. Has to do with -- has to do 20 with vitamin -- 21 MS. SHARKO: Let him finish. 22 THE WITNESS: Has to do with 23 vitamin C and the connection 24 between vitamin C and this pathway</p>
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<p>1 major work being done in the lab. 2 Q. In a nutshell, right? 3 A. Yes. 4 Q. Does your lab do both in 5 vitro and in vivo animal model research? 6 A. Yes. 7 Q. Do you do human research? 8 A. What do you mean by human 9 research? 10 Q. Anything that requires an 11 IRB, approval, the biomarkers in 12 patients, anything of that sort? 13 A. We have -- so IRB approval 14 is required to get issues and it's 15 usually a pretty standard -- what they 16 call administrative approval. So if 17 you're counting that, yes, we have 18 approval to get the tissues that we use 19 to make ovarian cancer xenographs. 20 We have a variety -- I 21 forgot to mention that we have a large 22 collection of ovarian cancer xenographs 23 in the lab that mainly came from my time 24 in Toronto. So we have hundreds of them.</p>	<p>1 that I mentioned to you of PP1B 2 and RNF213. 3 And we -- in reading the 4 literature on that, I realized 5 that there was a possible use of 6 vitamin C in myeloid dysplastic 7 syndrome and AML, and we got 8 together with some of my other 9 colleagues upstairs and did a 10 major paper that was published in 11 Cell last year and led to a 12 clinical trial. 13 So I'm helping the junior 14 faculty member in my department to 15 design that trial and to execute 16 it, which is running at the cancer 17 center right now. 18 So that's the only 19 connection. But I'm actually not 20 on that IRB, because I'm not 21 really doing the study. 22 BY DR. THOMPSON: 23 Q. Okay. And I -- I am not 24 intentionally interrupting you.</p>

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<p>1 Sometimes it's hard to tell when there's 2 a pause. Just so -- 3 A. I have to catch my breath, 4 you know. 5 Q. -- so you know that. 6 And the tissue samples that 7 you use, is that something that some 8 would refer to as ex vivo research? 9 A. So, you know, the use of the 10 word ex vivo is used pretty sloppily in 11 literature. Including some e-mails -- I 12 actually think it's confusing when to use 13 in vivo and not -- when to use in -- some 14 people use in vivo to refer to mice, to 15 mouse experiments. Some people don't. 16 Some people use in vivo 17 to -- some people -- I think what we can 18 all agree on is in vitro -- if it's a 19 pure biochemistry experiment where there 20 are no cells, that's in vitro. 21 Some people would then call 22 putting the same, you know, testing 23 agents on cells in vitro. Some would 24 call it in vivo.</p>	<p>1 going to shut down completely in two 2 months. 3 So if you call those ex 4 vivo, then that's ex vivo. But it's very 5 confusing nomenclature. So I prefer to 6 explain what we're actually doing, and 7 then you can judge what you want to call 8 it. 9 Q. And I'm glad to know I'm not 10 the only one that's confused, so... 11 A. I think it's sloppy, sloppy 12 wording. 13 Q. And you have published with 14 immortalized cell lines, correct? 15 A. Yes. 16 Q. As of most researchers in 17 the -- that are doing in vitro research, 18 correct? 19 A. Yes, but I -- the context is 20 important. And, you know, it's like -- 21 you use the right -- you have to -- if 22 you want to get definitive results or 23 interpretable results or convincing 24 results, you have to use the right cell</p>
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<p>1 And ex vivo, some people 2 would call taking cell -- taking human 3 cells out and doing the same kind of 4 studies that other people call in vitro. 5 So I can say what we do. 6 We -- as I told you, we make 7 organoids, which are these culture 8 systems that allow you to basically grow 9 the cells in much more physiologically 10 relevant settings involving extracellular 11 matrix and they form glands and things 12 like that. 13 We make organoids from 14 fallopian tube, from ovarian surface 15 epithelium of the mouse. And we have 16 done more limited work on making 17 fallopian tube organoids from the human. 18 We also have been involved 19 in studies, some of which will come out 20 soon in Nature Medicine, on the use -- on 21 developing organoid conditions for 22 culturing human ovarian cancers. And we 23 did that in my Toronto lab, which is 24 almost completely shut down. They are</p>	<p>1 system for the right experiment at the 2 right time. That's the point. 3 Q. What is contained in 4 Johnson's Baby Powder in your mind? 5 A. I -- I have no knowledge as 6 to what's in Johnson & Johnson's Baby 7 Powder. I'm not a chemist. I'm not a, 8 you know, material scientist, so... 9 Q. Do you even know what's on 10 the bottle as to what is contained? 11 A. No. 12 Q. And that doesn't matter to 13 you? 14 A. Not for the purpose of 15 writing my report, no. Or for examining 16 any of the studies that I referred to in 17 my report, no. It doesn't. 18 Q. Okay. And -- and would you 19 give the same answers for the Shower to 20 Shower product? 21 A. Yes. 22 Q. And it's your understanding 23 that Johnson & Johnson owns and 24 manufactures Johnson's Baby Powder,</p>

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<p style="text-align: right;">Page 70</p> <p>1 correct?</p> <p>2 MS. SHARKO: Object to the</p> <p>3 form of the question. Lacks</p> <p>4 foundation.</p> <p>5 THE WITNESS: So I have no</p> <p>6 idea what the business structure</p> <p>7 is that gives rise to Johnson &</p> <p>8 Johnson's Baby Powder.</p> <p>9 BY DR. THOMPSON:</p> <p>10 Q. Okay.</p> <p>11 A. All I know is that it's</p> <p>12 called Johnson & Johnson's Baby Powder.</p> <p>13 Q. Okay. And same answer for</p> <p>14 Shower to Shower?</p> <p>15 A. Yes.</p> <p>16 Q. Are you familiar with the</p> <p>17 various grades of talc?</p> <p>18 A. Not in any detail. I'm not</p> <p>19 a geologist.</p> <p>20 Q. And same answer that that</p> <p>21 doesn't -- isn't important to you as far</p> <p>22 as your opinions go in this case?</p> <p>23 A. No, because that wasn't what</p> <p>24 I was addressing in my report, nor what</p>	<p style="text-align: right;">Page 72</p> <p>1 would not know whether those claims would</p> <p>2 be misleading or not, correct?</p> <p>3 MS. SHARKO: Object to the</p> <p>4 form. Lacks foundation.</p> <p>5 THE WITNESS: No, I wouldn't</p> <p>6 have any knowledge of that.</p> <p>7 BY DR. THOMPSON:</p> <p>8 Q. Is it important for you to</p> <p>9 know the mineral content of a talcum</p> <p>10 powder product?</p> <p>11 A. Not for the purposes of my</p> <p>12 report, no.</p> <p>13 Q. Would it be important for</p> <p>14 you to know whether there are fibers or</p> <p>15 not in a talcum powder product to assess</p> <p>16 the potential health effects?</p> <p>17 A. Not for the purposes of my</p> <p>18 report which were to look at the specific</p> <p>19 issues that I've already covered.</p> <p>20 Q. And that goes for the</p> <p>21 opinions that you're giving today as</p> <p>22 well?</p> <p>23 A. Absolutely. Mm-hmm. My</p> <p>24 opinions that I'm giving today are based</p>
<p style="text-align: right;">Page 71</p> <p>1 I'm here to tell you about.</p> <p>2 Q. Do you know anything</p> <p>3 regarding the particle size of Johnson's</p> <p>4 Baby Powder or Shower to Shower?</p> <p>5 A. No.</p> <p>6 Q. Is it important for you to</p> <p>7 know the quality of a talcum powder</p> <p>8 product to assess its talc -- its health</p> <p>9 effects?</p> <p>10 A. No, not for the purpose of</p> <p>11 my report.</p> <p>12 Q. And would you describe</p> <p>13 quality as to the amount of and type of</p> <p>14 impurities in the talcum powder?</p> <p>15 A. I wouldn't describe quality</p> <p>16 because I am not qualified to discuss</p> <p>17 quality.</p> <p>18 Q. Does pure talc exist?</p> <p>19 A. I'm not a geologist. I have</p> <p>20 no opinion on that subject. I have no</p> <p>21 knowledge in that area. I'm a cancer</p> <p>22 biologist.</p> <p>23 Q. So if Johnson & Johnson</p> <p>24 makes claims that their talc is pure, you</p>	<p style="text-align: right;">Page 73</p> <p>1 on my report and any questions that you</p> <p>2 ask me.</p> <p>3 Q. So neither the type of</p> <p>4 fibers or the number of fibers is</p> <p>5 important in your -- in providing your</p> <p>6 opinions for us today?</p> <p>7 A. That's correct.</p> <p>8 Q. And you understand that this</p> <p>9 case involves women who use the Johnson &</p> <p>10 Johnson products in the genital area and</p> <p>11 subsequently developed ovarian cancer,</p> <p>12 correct?</p> <p>13 A. I assume so. I haven't read</p> <p>14 the complaint.</p> <p>15 Q. Okay. And when we talk</p> <p>16 about ovarian cancer generally, we're</p> <p>17 referring to epithelial ovarian cancer.</p> <p>18 Would you agree to that?</p> <p>19 A. Who is "we"?</p> <p>20 Q. You and I today.</p> <p>21 A. Yeah. Sure.</p> <p>22 Q. And I understand --</p> <p>23 A. But I don't -- but I don't</p> <p>24 think it's meaningful to talk about</p>

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<p>1 epithelial ovarian cancer anymore. 2 Not -- I mean, that entity is too 3 nondescript to be meaningful from a 2019 4 cellular molecular biology perspective. 5 Q. But you understand that that 6 is done in literature being published 7 every single day? 8 A. It's not done by people who 9 are familiar with the relevant molecular 10 and cellular data. There's lots of 11 papers published that aren't very good. 12 Q. And understanding that there 13 are different histologic types, as well 14 as the -- Type 1 and Type 2 being 15 described. And the field is obviously 16 evolving. Would you agree? 17 A. There were several -- 18 Q. There were. 19 A. Can you make it a more 20 specific question there? 21 Q. Yeah. 22 A. Because I don't necessarily 23 agree with everything that you said. So 24 if you break it down, maybe I can help</p>	<p>1 pretty much settled. But... 2 Q. But there is some debate 3 still as far as whether that applies to 4 some -- some ovarian cancers or all 5 ovarian cancers? 6 A. Well, all cancers have a 7 cell of origin. So I'm not clear what 8 your question is. 9 Q. Bad question. We'll move 10 on. 11 And there is certainly more 12 work being done with the histologic 13 subtypes and whether that's still a good 14 classification system, right? 15 A. I don't think that there is 16 any disagreement among modern ovarian 17 cancer researchers at the top 18 institutions and who are up on the 19 literature as to the fact that it's 20 nonmeaningful to talk about all ovarian 21 cancer or all epithelial ovarian cancer 22 any more than it's legitimate to talk 23 about all breast cancer or all many 24 different types -- lung cancer.</p>
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<p>1 get this. 2 Q. I think that's a good 3 criticism of that question. 4 The study of ovarian cancer 5 is an evolving field. Would you agree to 6 that? 7 A. Yes. 8 Q. And in fact, just a couple 9 years ago, National Academy of Science 10 Medicine and Engineering, supported by 11 CDC, sponsored a comprehensive study 12 entitled "Evolving Paradigms in Ovarian 13 Cancer." Are you familiar with that? 14 A. I remember reading it. 15 There's lots of review and things like 16 that. But yeah. 17 Q. And some of the areas that 18 are evolving would be the cell of origin 19 for ovarian -- epithelial ovarian cancer, 20 correct? 21 A. Yes. 22 Q. That's one of the things 23 that your lab is working on? 24 A. Yes. Although we think it's</p>	<p>1 They are separate molecular 2 diseases. Cancer is not a single 3 disease. Ovarian cancer is not a single 4 disease. And it's simply not meaningful 5 to talk about ovarian cancer or even 6 epithelial ovarian cancer. 7 In fact, I would say -- and 8 I would probably be going a little far, 9 but I would probably say that it's no 10 more meaningful to talk about ovarian 11 cancer as an entity than it is to 12 separate epithelial ovarian cancer from 13 germ cell cancers. They're different 14 cells of origin and they have different 15 molecular defects. 16 Q. How about at the patient 17 care level? 18 A. Well, that's one of the 19 problems at the patient care level, is 20 the patient care level hasn't caught up 21 with the molecular biology. And that's 22 the whole goal that what we're doing, 23 because it is ridiculous, in my opinion 24 to treat all ovarian cancer patients the</p>

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<p>1 same, and that's why we're not very good 2 at treating it. 3 Q. But there is still evolution 4 and debate in the field. Wouldn't you 5 agree? 6 MS. SHARKO: Object to the 7 form. 8 BY DR. THOMPSON: 9 Q. If we -- let's get out of 10 the molecular researchers at an elite 11 university and talk about medical or 12 gynecologic oncologists. You agree that 13 there is going to be a lag time between 14 what you're discovering and how that new 15 novel information gets transmitted and 16 utilized by doctors in the field? 17 MR. LOCKE: Objection to 18 form. 19 BY DR. THOMPSON: 20 Q. Correct? 21 A. So that's not -- I agree 22 that there's almost always a lag between 23 laboratory studies and implementation in 24 the clinic. I think that that's not a</p>	<p>1 having talked to women about how they use 2 talcum powder products in the perineal 3 area? 4 A. I think I'd get in trouble 5 if I had conversations with women about 6 that. I do have experience in using 7 talcum powder products, however. 8 Q. How is that? 9 A. When my -- I'm the oldest 10 brother of four boys. And my younger two 11 brothers, you know, are nine and 11 years 12 younger than I am. And as the oldest 13 boy, I was taught to diaper them. And 14 we -- they used -- I used talcum powder 15 products all the time on them. I would 16 dust their bottoms with the talcum powder 17 products. 18 Q. Would you currently dust 19 babies with talcum powder knowing what 20 you know? 21 A. I don't have any babies, so 22 I haven't given it any thought. I don't 23 have any reason to use it anymore. 24 Q. If someone asked you for</p>
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<p>1 good thing. And I should point out that 2 I am not just a laboratory researcher, 3 I'm the director of the Perlmutter Cancer 4 Center at NYU Langone. And my job is to 5 try to make sure that research, not just 6 in my lab but in other laboratories in 7 our institution, get translated as 8 quickly as possible in the form of 9 clinical trials at our institution and 10 elsewhere. 11 So I think that it is true 12 that modern information has not, you 13 know, transmitted to many people in 14 practice at other institutions. 15 But that doesn't mean that 16 the modern information isn't correct. 17 Q. And I did not mean to 18 diminish your role at all. 19 Do you have any 20 understanding of how the talcum powder 21 products are actually used by women? 22 A. I mean, only in the most 23 superficial and vague sense. 24 Q. So no firsthand knowledge</p>	<p>1 your advice? 2 A. Well, my daughter is 3 pregnant, so maybe I'll have to think 4 about it. But I wouldn't give any advice 5 on that. I'm not -- I'm not a medical 6 doctor. I don't really have any -- 7 everything is different about how diaper 8 goes now. 9 We used to use all kinds of 10 different stuff. I don't really remember 11 the details. But, you know -- 12 Q. So if -- 13 A. -- I don't remember if we 14 used talc on our girls or not. 15 Q. So if your daughter is 16 pregnant knows that you're -- you've 17 looked at this area, serving as an expert 18 for Johnson & Johnson, and asked you if 19 it was safe, would you recommend that she 20 use Johnson's Baby Powder with her new 21 baby, what would you tell her? 22 MR. LOCKE: Objection. 23 THE WITNESS: Well, my 24 daughter is -- can I answer that?</p>

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<p>1 My daughter who is pregnant 2 is an M.D. Ph.D. student at UCSF 3 and she wouldn't listen to me 4 anyway. 5 BY DR. THOMPSON: 6 Q. Well, that -- 7 A. She's a -- she's got her own 8 opinion. And she's got a Ph.D. in cancer 9 biology herself so she wouldn't -- she 10 would research it herself. So I wouldn't 11 waste the time in telling my daughter who 12 is a Ph.D. at UCSF, which is a better 13 medical school than we have here. 14 Q. Well, that may be true. 15 A. It is true. 16 Q. But if she did ask you, what 17 would you answer? 18 A. I would tell her that she 19 should look into it herself. 20 Q. Okay. And would that be the 21 same if the Baby Powder was shown to 22 contain asbestos? 23 MR. LOCKE: Objection. 24 THE WITNESS: I don't -- as</p>	<p>1 plausibility to those agents 2 causing ovarian cancer. That's 3 the basis of my report. And as I 4 understand it, that's why I am 5 here today, to provide testimony 6 on that basis. 7 BY DR. THOMPSON: 8 Q. And your opinion is there is 9 no biological plausibility to Baby Powder 10 products causing or contributing ovarian 11 cancer in the general sense? 12 A. Yes. I -- that is 13 definitely my opinion. In fact, if 14 anything, there's evidence that it 15 doesn't. 16 There's no evidence that it 17 does. And the available evidence 18 suggests that it doesn't. 19 Q. And you know that talcum 20 powder products are no longer used on 21 condoms or dusting diaphragms, correct? 22 A. I don't know that. 23 Q. Do you know that the FDA has 24 banned powdered medical exam gloves or</p>
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<p>1 I said, I wouldn't give anybody an 2 opinion on that. That's not my 3 place to give people opinions, so 4 it's -- I -- I don't know how to 5 answer your question. 6 BY DR. THOMPSON: 7 Q. Well, you are giving 8 opinions today -- 9 A. I'm giving -- 10 Q. -- as to what women should 11 do, right? 12 MS. SHARKO: Object to the 13 form. 14 THE WITNESS: No. No. 15 MS. SHARKO: Lacks 16 foundation. 17 THE WITNESS: I'm not giving 18 my opinion on what women should 19 do. Women should decide for 20 themselves what they should do. 21 I'm giving an opinion on 22 whether talc or Johnson & 23 Johnson's products, whether 24 there's any biological</p>	<p>1 surgical gloves? 2 MS. SHARKO: Object to the 3 form. Foundation. 4 THE WITNESS: I'm not an 5 expert in regulations that the FDA 6 might have. So I have no reason 7 to know one way or the other, nor 8 why they did it or didn't do it. 9 BY DR. THOMPSON: 10 Q. So in doing your research 11 for your report, was it irrelevant that 12 talcum powder was no longer used on exam 13 gloves or surgical gloves? 14 A. No, that wasn't relevant. 15 Because what I consider for my report was 16 the very clear issue of what, if any, is 17 the role of talcum powder products and/or 18 Johnson & Johnson products that contain 19 talc for ovarian cancer pathogenesis. 20 That was the basis of my 21 report and my reading and researching 22 related to this issue. 23 Q. As a physician would you 24 agree with me that there are no -- no</p>

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<p>1 known medical benefits from the use of 2 talcum powder products for hygiene 3 purposes? 4 A. As -- as you established 5 very early, I haven't seen a patient 6 since 1988 so I have no comment on that 7 as a physician. I'm not a -- I'm not a 8 practicing physician. 9 Q. So you don't know one way or 10 the other whether there are any medical 11 benefits? 12 A. I'm not aware of there being 13 any medical benefits. But I'm not in any 14 way current on the literature of, you 15 know, gynecology so -- or any other 16 possible use of talc. So I wouldn't 17 really feel comfortable giving an opinion 18 on something that I'm not an expert on. 19 As opposed to the issue of 20 whether talc causes ovarian cancer, which 21 is right in my area of expertise and I'm 22 quite confident in giving you an opinion 23 on that. 24 Q. Would the average layperson</p>	<p>1 think you told us before that you were 2 aware of some debate or discussion 3 regarding the safety of Baby Powder, did 4 anyone ask you to study that issue? 5 MS. SHARKO: Object to the 6 form. Lacks foundation. 7 THE WITNESS: No one asked 8 me to look at this before 9 Mr. Winter came to me. 10 But, you know, I want to -- 11 I'm not going to agree with the 12 premise of your question, because 13 I wasn't aware of a debate. 14 I think I said that I was 15 aware of reports in the press that 16 there was litigation. That 17 doesn't mean that there's a 18 debate. That just means there's 19 litigation, in my opinion. 20 BY DR. THOMPSON: 21 Q. Fair enough. 22 So prior to the reports in 23 the news over the past few years, you 24 weren't aware of any concerns about Baby</p>
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<p>1 know that there are no medical benefits 2 from using Baby Powder? 3 A. I have no idea what the 4 average layperson does. 5 As I say, I don't see 6 patients. So I don't really have any way 7 to assess what the average layperson's 8 knowledge is or isn't of talc products. 9 Q. Would the average layperson 10 understand that there are different 11 molecular subtypes of ovarian cancer? 12 A. Almost certainly not, since 13 I find that many gynecological 14 oncologists don't, you know, in the 15 community. 16 Q. Prior to being contacted 17 regarding serving as an expert in this 18 litigation, did Johnson & Johnson, or 19 anyone for that matter, ever contact you 20 to explore the relationship between 21 talcum powder and ovarian cancer in your 22 laboratory? 23 A. No. 24 Q. And over 39 years, and I</p>	<p>1 Powder in the '70s, '80s, going forward? 2 A. No. I wouldn't -- no. 3 Not -- not -- I only read about things 4 about -- you know, regarding talc since 5 Mr. Winter came to me in May of 2017. 6 Q. And you weren't -- you 7 weren't aware of any concerns about Baby 8 Powder or talcum powder containing 9 asbestos? 10 A. I -- I read things about 11 that in the course of doing my research 12 on this topic. But I wasn't aware of it 13 before. 14 Q. So prior to being consulted, 15 you were not aware of any concerns -- 16 A. Correct. 17 Q. -- about Baby Powder. 18 I think we've answered this. 19 But other than the literature and 20 document review, you have not done any 21 research on the -- on talcum powder and 22 ovarian cancer, correct? 23 A. Just to clarify. I did do 24 one type of research, which is computer</p>

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<p>1 research which is in my report. And I 2 want to make sure that I'm not misstating 3 that. 4 I did, you know, for 5 example, test the validity of some of 6 Dr. Saed's claims by just doing simple 7 searches on publicly available websites, 8 some of which were the websites that were 9 cited there. So I don't know if you 10 count that as research. But other than 11 that, no. 12 Q. Okay. Have you discussed 13 your opinions in this case with anyone 14 else? 15 A. No. 16 Q. You have not discussed your 17 opinions with any colleagues? 18 A. None -- I mentioned that I 19 was participating in this case, but other 20 than that I have not discussed my 21 opinions on this -- I probably discussed 22 them with my wife. But that's 23 privileged. 24 Q. I'm not sure it is. But</p>	<p>1 Q. I believe she participated 2 in one of the conferences where -- 3 A. I'm sure she did. 4 Q. -- you were program 5 director? 6 A. I haven't met her 7 personally. I know who she is. 8 Q. Okay. And does that mean 9 that you have not discussed the case with 10 Liz -- Dr. Swisher? 11 A. I have definitely not 12 discussed the case. I don't know. So I 13 couldn't discuss it. 14 Q. I understand. 15 You brought with you today 16 invoices that you had submitted to 17 Johnson & Johnson, correct? 18 A. I didn't bring anything with 19 me today. 20 Q. Someone did. 21 A. Okay. 22 Q. But let me give you a copy 23 of the invoice marked as Exhibit 6. 24 (Document marked for</p>
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<p>1 we'll -- we'll give you a pass on that 2 one. 3 A. Okay. Actually I was asked 4 by -- last night, my -- there were people 5 in my house, and I said I can't discuss 6 this, so -- she told me I had to go to 7 sleep. 8 Q. You told -- you mentioned 9 that you had told -- is that colleagues 10 that you've told that you're working on 11 the case? 12 A. I had explained why I wasn't 13 going to be here today. So -- and I had 14 to explain why I wasn't going to be 15 here -- why I went to the lawyers' 16 offices several times in the last couple 17 of weeks, so yes. 18 Q. Okay. Did you discuss any 19 details as far as your opinions -- 20 A. No. 21 Q. -- in the case? 22 Do you know Liz Swisher? 23 A. I don't know her personally. 24 I know her name, yes.</p>	<p>1 identification as Exhibit 2 Neel-6.) 3 BY DR. THOMPSON: 4 Q. Does this appear to be -- 5 this document appear to be invoices that 6 you've submitted? 7 A. Yes. 8 Q. And did you prepare these 9 invoices yourself? 10 A. Yes. 11 Q. And it looks to me that 12 you've worked on the case about 13 122 hours. Does that sound about right? 14 A. Probably. This doesn't even 15 include the latest invoice. So it's a 16 little bit more. Maybe 140 hours, 17 150 hours, something like that. 18 Q. And you're billing at \$750 19 an hour. 20 A. Yes. 21 Q. Correct? 22 What did you do to prepare 23 for your deposition today? 24 A. What did I do? I re-read</p>

24 (Pages 90 to 93)

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<p>1 some of the papers. I read my report. I 2 read some of the expert reports. And I 3 had, as I just alluded to, several 4 discussions with Ms. Sharko and 5 Mr. Zellers. 6 Q. Did you meet -- when did you 7 meet with the attorneys? 8 A. I'd have to check my 9 calendar to get the exact dates. You 10 know, I have so many things to keep in my 11 head, I only try to retain the stuff 12 that's material. 13 Q. Has it been in the last few 14 days? 15 A. I met with them very briefly 16 yesterday. But yes, there have been a 17 couple of conferences. 18 Q. And for how long did you 19 meet yesterday? 20 A. An hour and a half maybe. 21 Maybe a little less. 22 Q. Let's go to your report now. 23 I didn't see a section of your report 24 that describes the methodology that you</p>	<p>1 that's trying to study the same issue 2 replicate what you did to formulate their 3 own opinions? 4 A. Well, the first thing they 5 could do is go to graduate school and 6 medical school, medical residency, 7 postdoctoral fellowship, and have 8 30 years in cancer biology. That would 9 be the background that you would need to 10 have my opinions in this report. 11 And assuming that you found 12 someone with that degree of training and 13 expertise, they would almost certainly do 14 exactly what I did. 15 Q. As you described reading the 16 references, searching for additional 17 references and then relying on your 39 -- 18 is it 39 years of experience? 19 A. I don't know. You'd have to 20 count it. It's very depressing for you 21 to keep repeating that number. 22 Q. That is the first time I've 23 repeated it. 24 A. That's the second time.</p>
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<p>1 used to reach your opinions. Can you 2 describe for me as best you can how you 3 formulated the opinions that you gave in 4 your report? 5 A. I read references that are 6 listed in the report, consulted some 7 additional references that I found were 8 not material. I did the searches that I 9 explained earlier on GWAS.org and also on 10 the Sanger website and the CCLE website 11 at the Broad. 12 And I read the other expert 13 reports and some of their papers, and I 14 came up with my opinions. 15 Q. Can you refer me to a 16 published article or textbook chapter or 17 treatise or anything that actually 18 describes the methodology that you used 19 in formulating your opinions and writing 20 your report? 21 A. I don't think there is a 22 textbook that tells scientists how to 23 arrive at opinions. 24 Q. How would someone else</p>	<p>1 Q. Is it the second time? 2 Sorry about that. 3 A. I said it once, and that was 4 depressing enough. 5 Q. I'm afraid that I have more 6 experience -- or years than that. 7 But did you use the same 8 standards in reaching the opinions in 9 your report that you would use, for 10 example, if you were publishing a paper? 11 A. Yeah, I think that's 12 actually a good analogy. This is very 13 similar to a type of strategy that I 14 would use if I were writing a review 15 article. So I've written about 37 -- or 16 co-authored 37 review articles, or a book 17 chapter. That's the kind of approach 18 that I would use there. Very, very 19 similar. I should have said that 20 actually. That's a very good analogy. 21 Q. Oh, you're welcome. 22 Did you do a comprehensive 23 literature review on all relevant topics? 24 A. I did -- as I think I would</p>

25 (Pages 94 to 97)

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<p>1 actually answer now the way you just 2 helped me answer, because I think that's 3 what -- I reviewed this to the degree of 4 depth that I would write an article on. 5 If I were going to write a review on 6 ovarian cancer and talc for a scientific 7 publication, this is the approach that I 8 would use.</p> <p>9 Q. Did you do any comprehensive 10 review on fibers and particles and their 11 role in carcinogenesis? 12 A. No. 13 Q. Did you do any literature 14 review on asbestos? 15 A. Only a very limited amount 16 of review of asbestos in the context of 17 ovarian cancer. 18 Q. Did you do any review on 19 fibrous talc? 20 A. Not that I recall. Only in 21 the context of it might have been 22 mentioned in some of the papers that I 23 reviewed. 24 Q. What is fibrous talc?</p>	<p>1 So I don't know how to 2 describe it any better than that. It's 3 very similar to the strict approach that 4 we would use for evaluating a new paper 5 we got to review. 6 And that's the same standard 7 that I use when writing a review article. 8 I go to the literature, I read the papers 9 thoroughly, I don't take the conclusions 10 or the statements of the authors at face 11 value. I look to see whether the data 12 supports it -- whether the data support 13 it, and then I reach a conclusion, and 14 I -- I put that in the review in the 15 context of my evaluation of the paper. 16 And that's what I did here. 17 Q. So as far as weighing the 18 evidence, would you agree that it's kind 19 of a gestalt, based on your education and 20 experience? 21 MS. SHARKO: Object to the 22 form of the question. 23 THE WITNESS: Can you define 24 gestalt? Because I know people</p>
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<p>1 A. I can't describe. I'm not a 2 geologist. I'm a cancer biologist. 3 Q. Did you use the particular 4 method to weigh the evidence from the 5 literature? 6 A. I -- it's very hard -- you 7 know, it's very hard to describe how a 8 scientist evaluates data. We have a lot 9 of training in terms of looking at data 10 and assessing its strengths and 11 weaknesses and coming to a conclusion 12 about that. 13 For example, I am an editor 14 of six -- I'm on the editorial board of 15 six major cancer journals. I review 16 papers all the time. I'm reviewing a 17 paper right now, for example, in one of 18 the other areas, not in ovarian cancer, 19 but one of the other areas that I 20 mentioned earlier. And I applied the 21 same standard to reviewing this 22 literature that I would apply to 23 reviewing a manuscript for Cell, Science, 24 Nature, all of these major journals.</p>	<p>1 use that in the common parlance. 2 And I want to make sure we're 3 being accurate, since it's on the 4 record and I'm testifying. 5 BY DR. THOMPSON: 6 Q. How would -- in the way that 7 you would define it. 8 A. I think it's more like what 9 Potter Stewart said about pornography. 10 You know it when you see it, and I know 11 that the studies that I read on the 12 biological plausibility of talc are bad. 13 And I can state exactly why they're bad 14 in multiple ways. I think I did in my 15 report. 16 Q. Yeah, and I'm sure you are 17 going to have more opportunity. 18 But would you say it's more 19 subjective than objective? 20 A. No, I would say it's quite 21 the contrary. It's quite objective. Bad 22 science is very objective. People who 23 are trained in the art can tell it. 24 Q. But I'm talking about the</p>

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<p style="text-align: right;">Page 102</p> <p>1 methodology, the objective methodology. 2 A. I'm trying as best I can to 3 explain the methodology. 4 You read the paper, okay. 5 You look at the data. You see if the 6 data supports the claims. Okay. And 7 unfortunately, in many journals, the data 8 doesn't support the claims, even though 9 the authors say it supports the claims. 10 So, you know, there is a lot 11 of papers that are published that either 12 overstate their data or provide evidence 13 that is not rigorous and they still get 14 published, because, you know, there's a 15 paper for every journal and a journal for 16 every paper, as my mentor once said. 17 Q. And that process is using 18 your professional judgment I assume, 19 right? 20 A. I think judgment is a little 21 soft there. It's using my professional 22 experience. 23 Q. Experience. 24 A. And -- experience and</p>	<p style="text-align: right;">Page 104</p> <p>1 A. Absolutely. 2 Q. Did you perform a Bradford 3 Hill analysis to determine causation in 4 this case? 5 A. Well, I'm not an 6 epidemiologist. Bradford Hill criteria 7 are epidemiological criteria. I did, you 8 know, read -- in the course of doing my 9 research, I did read the Bradford Hill 10 paper, and I did address several of the 11 issues that Bradford Hill addressed. 12 But, you know, as I said, 13 my -- my expertise, as I think you know, 14 is primarily in the area of cancer 15 biology. And, you know, I did read the 16 epidemiological literature from the 17 standpoint of someone who is trained as a 18 physician and also who is in charge of 19 running the epidemiology and cancer 20 control program for our cancer center 21 grant. So I do have a little -- I have 22 the ability to read that, but my 23 expertise is primarily the cancer biology 24 expertise. And that's where I -- I feel</p>
<p style="text-align: right;">Page 103</p> <p>1 judgment. 2 Q. And judgment. 3 A. Yes. 4 Q. Okay. 5 A. And training. I mean, you 6 know, I've been doing this for a while. 7 Q. 39 years, right? 8 A. See, you're just doing that 9 to upset me. It's not fair. It's not 10 fair to upset the witness. 11 Q. You know I'm going to get 12 that in every time I can from now on. 13 A. I'm going to have to 14 calculate to see if it really is 39. It 15 might be 38. 16 Q. Regarding the report, do you 17 intend to write up your opinions as to a 18 review article in this case? 19 A. I hadn't thought of doing 20 it, no. But... 21 Q. But you'd be willing to 22 submit your report to -- for peer review? 23 A. Sure. 24 Q. Is that a fair assumption?</p>	<p style="text-align: right;">Page 105</p> <p>1 I have the most definitive training and 2 expert and -- and knowledge. 3 Q. So I think you'd agree that 4 you are not an epidemiologist, per se? 5 A. No, I'm not an 6 epidemiologist. I think I stated that. 7 Q. And -- and you don't hold 8 yourself out to be an epidemiologist -- 9 A. No. 10 Q. -- correct? 11 Have you ever performed a 12 Bradford Hill analysis in the course of 13 your work as a cancer biologist? 14 A. No. 15 Q. Do you agree that scientists 16 can look at the same body of literature 17 and reach different conclusions? 18 A. Sometimes. 19 Q. And that's in a general 20 sense, I'm asking that question. 21 A. Sometimes. But not often. 22 Q. So -- so credible and 23 qualified scientists don't always agree. 24 Would you say that's right?</p>

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<p style="text-align: right;">Page 106</p> <p>1 A. When they don't agree, 2 that's because the data aren't strong 3 enough to reach agreement. The essence 4 of science is that it's empirical, which 5 means that people can make the same 6 observations in different places at 7 different times when using the same 8 methods. And they can, therefore, reach 9 the same conclusion. 10 When scientists disagree, 11 it's because the science is not settled. 12 Q. And you would agree that 13 there are often debates in medicine and 14 science? 15 A. I would answer the question 16 the same way I just answered. That when 17 there are debates in medicine and 18 science, it's because the science has not 19 established to a reasonable scientific 20 certainty that something is or isn't 21 true. 22 Q. And it's your opinion in 23 this case regarding the relationship 24 between the genital use of talcum powder</p>	<p style="text-align: right;">Page 108</p> <p>1 Q. You -- I just want to make 2 clear. 3 So in your opinion, the 4 science has settled that there's no 5 association, correct? 6 A. You -- you can't -- in 7 science you can't prove a negative. 8 So -- you can only prove a positive. And 9 I will restate my opinion, because that's 10 my opinion. 11 There is no credible 12 scientific evidence that perineal talc 13 causes ovarian cancer at all. There's no 14 evidence. 15 Q. Leave out the credible. Is 16 there no evidence? 17 A. In science there is no such 18 thing as incredible -- incredible 19 evidence. There's evidence and there's 20 bad science. 21 Q. Okay. 22 A. So if you'd like me to say 23 that there's bad science that claims that 24 ovarian cancer is caused by talc, I guess</p>
<p style="text-align: right;">Page 107</p> <p>1 and ovarian cancer, that the science is 2 settled? 3 A. No. It is my opinion that 4 there is no scientific evidence to 5 support the contention that talc applied 6 perineally causes ovarian cancer. There 7 is -- 8 Q. So the science is not 9 settled? 10 MS. SHARKO: Wait, wait. 11 Let him finish his answer. 12 DR. THOMPSON: You don't 13 have to remind me every time -- 14 when I do it, it's unintentional. 15 And I will pause as soon as I see 16 that he's going to continue to 17 talk. 18 BY DR. THOMPSON: 19 Q. Go ahead, Dr. Neel. 20 A. There is no -- the available 21 evidence does not support to any 22 scientific credibility that perineal talc 23 causes ovarian cancer. That is my 24 opinion.</p>	<p style="text-align: right;">Page 109</p> <p>1 I could say that. It's bad science. 2 Q. And I don't want you to say 3 anything. I just want -- want you to 4 give what your opinions are. 5 A. No, there is no credible -- 6 there is no credible scientific evidence 7 that perineal talc causes ovarian cancer 8 in my opinion. 9 DR. THOMPSON: I'm at a 10 breakpoint if that -- if this is a 11 good time for -- for you, Doctor? 12 THE WITNESS: Sure, I was 13 just going to say. I think that 14 would be good actually. 15 THE VIDEOGRAPHER: Remove 16 your microphone. The time is 17 10:21 a.m. Going off the record. 18 (Short break.) 19 THE VIDEOGRAPHER: We are 20 back on the record. The time is 21 10:40 a.m. 22 BY DR. THOMPSON: 23 Q. Dr. Neel, looking at your 24 report, Page 8, you have a section that</p>

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<p>1 speaks of the hallmarks of cancer with a 2 reference to Dr. Hanahan's paper, 2011, 3 titled "Hallmarks of Cancer." And that's 4 just been marked as Exhibit 8. 5 (Document marked for 6 identification as Exhibit 7 Neel-8.) 8 BY DR. THOMPSON: 9 Q. You'll agree that this is a 10 classic paper in the field of cancer 11 biology, wouldn't you? 12 A. Yeah, it's a review article, 13 but yes. 14 Q. And -- right, a review 15 article. It does -- it's not reporting 16 primary research. 17 And reading in the abstract, 18 talking about the hallmarks of cancer 19 which include sustaining proliferative 20 signaling, evading growth suppressors, 21 resisting cell death, enabling 22 replicative immortality, inducing 23 angiogenesis, and activating invasion and 24 metastases.</p>	<p>1 A. Because the hallmarks are 2 the things you read. As it says, 3 underlying these hallmarks are certain 4 things. But the reason is that -- so 5 again, you have to distinguish between 6 inflammation that accompanies cancer and 7 those cancers that have a component of 8 inflammation in their initiation. I 9 think that's what we are talking about 10 here. 11 And there is no evidence 12 that ovarian cancer, or at least serous 13 cancers, which is the major topic here, 14 have inflammation as part of their, you 15 know, initiation phase. And there's 16 evidence against it. 17 Q. So it's your opinion that 18 inflammation does not play a role in the 19 initiation of ovarian cancer? 20 A. Yes. 21 Q. And you would -- 22 A. In high grade serous ovarian 23 cancer. 24 Q. And you would agree that</p>
Page 111	Page 113
<p>1 Did I read that correctly as 2 far as the hallmarks? 3 A. Yes. 4 Q. With some difficulty. 5 MS. SHARKO: Wait, wait. 6 Where are you reading from? 7 THE WITNESS: She's right 8 there. 9 MS. SHARKO: Oh, you are 10 reading from the paper. 11 THE WITNESS: Reading from 12 the text. 13 MS. SHARKO: Okay. 14 BY DR. THOMPSON: 15 Q. And then the next sentence, 16 "Underlying these hallmarks are genome 17 instability which generates the genetic 18 diversity that expedites their 19 acquisition, and inflammation, which 20 fosters multiple hallmark functions." 21 Why did you not mention 22 inflammation in your description of the 23 cancer hallmarks as reported by Hanahan 24 in his review article, 2011?</p>	<p>1 there are certainly other cancer 2 researchers that would disagree with that 3 opinion, correct? 4 A. I don't know who 5 specifically you're talking about. But I 6 would -- I'm happy to go over, you know, 7 whatever particular, you know, opinion 8 you are talking about. 9 Q. So you're not aware of any 10 scientist that would have the opinion 11 that inflammation can play a role in the 12 pathogenesis of epithelial ovarian 13 cancer? 14 A. No, I didn't say that. 15 MR. LOCKE: Objection to 16 form. 17 THE WITNESS: I didn't say 18 that. 19 There's clearly -- am I -- 20 MS. SHARKO: Answer. Go 21 ahead. 22 THE WITNESS: She's not 23 looking. So I assumed. 24 BY DR. THOMPSON:</p>

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<p>1 Q. I just wanted to make sure I 2 asked the right question. And I think I 3 did, so -- 4 A. Okay. There's clearly 5 inflammation in ovarian cancer. But that 6 doesn't mean that inflammation is 7 involved in the initiation of ovarian 8 cancer, which is the issue under study 9 here. Okay. 10 Q. And my question was about 11 the initiation. 12 A. Okay. So in the context of 13 high grade serous cancer, there is no 14 compelling evidence that there is any 15 inflammation involved in that process. 16 If you look at -- we now know, and again 17 this is relatively recent information. 18 But in the last 15 years or 19 so, it's becoming increasingly clear that 20 there are very well-defined 21 pre-neoplastic lesions on the fallopian 22 tube called STICs, which stands for 23 serous tubular intraepithelial 24 carcinomas -- and in serous tubal</p>	<p>1 which was not possible previously. 2 DR. THOMPSON: Object as 3 nonresponsive. 4 BY DR. THOMPSON: 5 Q. Because my question was, are 6 there other scientists who would disagree 7 that inflammation does not play a role in 8 the pathogenesis of ovarian cancer? 9 A. Well, again, in the -- I 10 don't think there's anybody who would 11 disagree with the statement that I just 12 made. Okay. 13 I think that when -- there's 14 definitely inflammatory responses to the 15 cancer. Okay. And cancer does play -- 16 inflammation does play a role in the 17 pathogenesis of ovarian cancer from the 18 standpoint of when you have a fully 19 developed ovarian cancer, whether there's 20 inflammation present, and to what type of 21 inflammation will affect clinical 22 response and also survival. 23 That doesn't mean that 24 inflammation is causal to ovarian cancer.</p>
Page 115	Page 117
<p>1 intraepithelial carcinomas -- and there's 2 earlier lesions that can be seen, called 3 STILs or p53 signatures. 4 And those have been studied 5 pathologically by Malmberg, et al. and 6 also by, you know, Dr. Shi, whose 7 report -- expert report I did, has done 8 an independent -- I read, has done an 9 independent assessment. 10 And if you look in those 11 lesions, there's no evidence of 12 inflammation. So that's -- we know for 13 sure that those lesions are 14 pre-neoplastic. 15 So we have actually, since 16 the discovery of these lesions and the 17 underlying molecular pathogenesis that 18 accompanies these lesions, we're able to 19 say with quite a bit of scientific 20 confidence that they are pre-neoplastic 21 and in the case of STICs, the first stage 22 in ovarian cancer. 23 So we actually can see 24 snapshots of the initiation process,</p>	<p>1 And I think that's where maybe there's 2 some confusion. 3 Q. Would you agree that 4 carcinogenesis usually refers to, not 5 only the initiation, but the promotion 6 and progression of cancer? 7 A. Yes. But I think that, 8 again, the cancer is present from the 9 standpoint once you have a STIC. So that 10 is a cancer. 11 Q. So if there were scientists 12 that did believe that inflammation plays 13 a role in the pathogenesis of ovarian 14 cancer, not -- not limiting that to just 15 the initiation, would they just be wrong? 16 A. I can't respond to a 17 hypothetical question like that without 18 seeing exactly what we're talking about. 19 So if you want to show me the actual 20 context of the statement, I'm happy to 21 offer an opinion one way or the other 22 about that. But I can't respond to a 23 sort of, with respect, somewhat vague 24 hypothetical about scientists of -- that</p>

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<p>1 aren't specified and exactly what they 2 said. 3 Q. How about other subtypes 4 besides serous? 5 A. Yeah, again, the -- there 6 are data that, for example, pelvic 7 inflammatory disease may be involved in 8 some forms of low grade serous cancer. 9 But there it's not clear if it's the 10 inflammation or the agent itself. And 11 the recent data would suggest it's 12 probably a specific agent there as 13 opposed to inflammation, per se. 14 Q. Back to the Hanahan article, 15 Page 658, "Emerging Hallmarks." And his 16 paper does not deal exclusively with 17 ovarian cancer. You'll agree, correct? 18 A. Correct. 19 Q. Under the chart, "Emerging 20 Hallmarks," he does list -- it's a he? 21 A. Yeah. It's 22 Hanahan/Weinberg. I'm sure Bob Weinberg 23 would be very insulted if you thought 24 that he was --</p>	<p>1 cancer? 2 MS. SHARKO: Object to the 3 form. Misstates his testimony. 4 THE WITNESS: Yeah, again, 5 what I said before, was there's no 6 question that inflammatory cells 7 are involved in fully blown 8 ovarian cancer. 9 If you look at a full -- if 10 I take an ovarian cancer from a 11 patient, it will have between 20 12 and sometimes up to 85 or 13 90 percent inflammatory cells. 14 So there's no question that 15 the body tries to respond to the 16 cancer with an inflammatory 17 response. But that's not the same 18 as saying that inflammation is 19 involved in the pathogenesis of 20 ovarian cancer. 21 For example, like 22 inflammation is clearly involved 23 in the pathogenesis of gastric 24 cancer caused by H. pylori.</p>
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<p>1 Q. Yeah, I thought so. But 2 I -- a lot of our other papers are 3 written by women. 4 And there is an emerging 5 hallmark described as tumor-promoting 6 inflammation. And you would agree that 7 tumor-promoting inflammation is an 8 emerging hallmark, correct? 9 A. In certain cancers, 10 inflammation plays a very important rule. 11 There's no evidence that that's for 12 ovarian cancer. No compelling -- 13 Q. But you would agree that 14 other scientists have published that 15 inflammation does play a role in ovarian 16 cancer, correct? 17 A. Again, I'm not sure what 18 exact publications that you're referring 19 to and in what context. So I can't 20 comment on a vague question like that. I 21 need to see the actual statement. 22 Q. So you're not aware of any 23 literature where it is published that 24 inflammation plays a role in ovarian</p>	<p>1 So you have to -- you know, 2 you have to consider the 3 specifics, which is why I can't 4 comment on your, you know, 5 question about other scientists 6 and inflammation. I need to see 7 the actual claim. 8 BY DR. THOMPSON: 9 Q. Okay. Are the inflammatory 10 pathways outlined in the Hanahan study 11 plausible? 12 A. Which inflammatory pathways 13 are you talking about? 14 Q. The one that he describes -- 15 A. Where -- where are you in 16 the -- okay. So, for example, on page 17 664, immune inflammatory cells -- 18 I'm sorry. I lost my 19 microphone. 20 Let's -- if you go to Page 21 664, under the title "Immune Inflammatory 22 Cells." 23 "Also, as discussed above, 24 infiltrating cells of the immune system</p>

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<p>1 are increasingly accepted to be generic 2 constituents of tumors." That's exactly 3 what I said. Okay. They are generic 4 constituents of tumors. That does not 5 speak to the initiation event. And again 6 these inflammatory cells operate in 7 conflicting ways, both tumor antagonizing 8 and tumor promoting -- 9 MS. SHARKO: You have to 10 read a little slower. 11 THE WITNESS: Oh, I'm sorry. 12 I switch into fast mode when I'm 13 reading. 14 MS. SHARKO: That's okay. 15 THE WITNESS: "These 16 inflammatory cells operate in 17 conflicting ways. Both 18 tumor-antagonizing and 19 tumor-promoting leukocytes can be 20 found in various proportions, if 21 not in most, all neoplastic 22 lesions." 23 So that's -- that's exactly 24 what I said before. The cancer --</p>	<p>1 A. No. Again, this was a 2 general -- 3 Q. That's a yes-no question. 4 You left that out of your report, right? 5 A. I didn't discuss it in 6 that -- in that particular place in my 7 report. 8 Q. Okay. Let's go to another 9 general cancer article. 10 You are familiar with 11 Dr. Balkwill I'm sure? 12 A. Yes. 13 Q. And Dr. Balkwill, I think, 14 was a featured speaker at one of your 15 conferences -- 16 A. I know Fran personally. 17 Q. -- and you know her. 18 A. Yes. 19 Q. Do you respect her as a 20 credible scientist? 21 A. Yes. 22 DR. THOMPSON: I'm going to 23 mark Dr. Balkwill's review 24 article.</p>
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<p>1 there is no question that when you 2 have a cancer developing, that the 3 cell -- the body tries to respond 4 to it usually. And depending on 5 the nature of the response, that 6 response can antagonize the tumor 7 or it can help the tumor, because 8 the tumor adapts ways to respond 9 to it in a positive way. 10 BY DR. THOMPSON: 11 Q. And -- 12 A. But that's not initiation. 13 Q. Yeah, that wasn't my 14 question either. 15 A. Okay. 16 Q. But you will agree that in 17 using this review article to describe the 18 hall -- hallmarks of cancer, and it 19 wasn't a specific discussion of ovarian, 20 it was a discussion of all cancers, you 21 left out the -- several places in the 22 Hanahan report where the authors discuss 23 inflammation and its role in cancer, 24 correct?</p>	<p>1 (Document marked for 2 identification as Exhibit 3 Neel-9.) 4 MS. SHARKO: Do we have an 5 Exhibit 7? This is Exhibit 9, 6 right? 7 MR. ZELLERS: Yes, it should 8 be 9. The last one was 8. 9 (Whereupon, a discussion was 10 held off the record.) 11 DR. THOMPSON: I don't have 12 a 7 sticker. But we'll -- we'll 13 figure that out at the break. 14 BY DR. THOMPSON: 15 Q. Are you familiar with this 16 article -- 17 A. Yes. 18 Q. -- titled, "Inflammation and 19 cancer: Back to Virchow?" 20 A. Yes. Virchow. 21 Q. Virchow, sorry. 22 And this article, reading 23 from the abstract again, "Reviews the 24 links between cancer and inflammation and</p>

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<p style="text-align: right;">Page 126</p> <p>1 discusses the implication of these links 2 for cancer prevention and treatment. We 3 suggest that the inflammatory cells and 4 cytokines found in tumors are more likely 5 to contribute to tumor growth, 6 progression, and immunosuppression than 7 they are to mount an effective host 8 anti-tumor response. Moreover cancer 9 susceptibility and severity may be 10 associated with functional polymorphisms 11 of inflammatory cytokine genes, and 12 deletion or inhibition of inflammatory 13 cytokines inhibits development of 14 experimental cancer. 15 "If genetic damage is the 16 'match that lights the fire' of cancer, 17 some types of inflammation may provide 18 the 'fuel that feeds the flames.'" 19 Would you agree with that 20 statement that Dr. Balkwill made in this 21 review article? 22 A. Which statement? There's a 23 number of statements there. 24 Would I agree with all of</p>	<p style="text-align: right;">Page 128</p> <p>1 inflammation and cancer risk. 2 Cancer risk would be the 3 cause or the initiation of cancer, right? 4 A. I'm not sure what she meant 5 there. But generally that's true. 6 Q. You wouldn't refer to risk 7 of -- when you have a cancer that's 8 already there, would you? 9 A. No, definitely not. 10 Q. And doctor -- 11 A. But actually in the -- can I 12 finish my statement? 13 But in the context of the 14 fact that cancer is a genetic disease and 15 the genetic damage that causes cancer is 16 what lights the fire, I think she's 17 actually said that this is not involved 18 in cancer initiation because this fuels 19 the flames. 20 So if you use her own 21 language, I think it supports my position 22 on this subject which has actually 23 developed much more since 2001. 24 Q. And I'm looking at</p>
<p style="text-align: right;">Page 127</p> <p>1 it? 2 Q. Would you agree with all of 3 that? 4 A. Insofar as it generally says 5 what's true in cancer in general, yes. 6 Insofar as it refers to specific issues 7 that are raised in my report and in my 8 testimony thus far, not completely. 9 And I would also note that 10 this paper is from 2001 which basically 11 makes it ancient history. 12 Q. And if you -- 13 A. Just so you -- can I just 14 complete that? 15 There's been more learned 16 about ovarian cancer in the last ten 17 years than in all of reported history 18 before then. So really, citing papers 19 from 2001 are really not relevant to 20 current ovarian cancer pathogenesis or 21 what our knowledge is of current ovarian 22 cancer pathogenesis. 23 Q. Looking at the chart, 24 Panel 1, some associations between</p>	<p style="text-align: right;">Page 129</p> <p>1 Panel 1 -- 2 A. Yes. 3 Q. -- some associations between 4 inflammation and cancer risk. 5 A. Mm-hmm. 6 Q. And it does list ovarian -- 7 A. Yes, it does. 8 Q. -- correct, in this chart? 9 A. Mm-hmm. 10 Q. And the inflammatory 11 stimulus or condition is listed as pelvic 12 inflammatory disease, talc, tissue 13 remodeling. 14 A. Mm-hmm. 15 Q. Is Dr. Balkwill wrong about 16 that? 17 A. Yes. She is incorrect 18 according to modern knowledge, yes, on 19 those details. 20 Q. Despite -- 21 A. The tissue remodeling is 22 probably correct. The other two are 23 unclear. More recent evidence does 24 suggest a possible connection with pelvic</p>

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<p style="text-align: right;">Page 130</p> <p>1 inflammatory disease, as I already said. 2 But that's very -- very recent, hasn't 3 been firmly established yet. 4 And, in fact, the 5 conclusions of the articles that -- that 6 discuss the risk of pelvic inflammatory 7 disease state that more research is -- is 8 needed. 9 And I'm actually quite 10 interested in the recent abstract that 11 was at last year's ACR, I want to see if 12 the paper comes out on Chlamydia 13 trachomata and serous cancers, because 14 that would actually be quite interesting 15 as it would tie ovarian cancer 16 pathogenesis to a specific agent, which 17 has not been done before. 18 Q. And -- and -- 19 A. There is increasing evidence 20 that specific infectious agents are 21 actually relevant in various cancers. So 22 that would be interesting. 23 The talc data was quite 24 immature in 2001 so I don't really think</p>	<p style="text-align: right;">Page 132</p> <p>1 form. 2 THE WITNESS: So there's two 3 questions there. Can we break 4 them in half? 5 You said I've already 6 testified as to this. 7 What I testified to is that 8 I considered whatever was defined 9 as talc in the papers that I read. 10 And in some cases, specific talc 11 was defined as Johnson & Johnson 12 talc. 13 In others, it was just 14 generic talc. In still others it 15 was defined as, for example, talc 16 from Sigma. 17 We'd have to go through 18 every single paper to see what 19 talc was used in the particular 20 study. Some of the studies also 21 used a mixture -- not a mixture, 22 but they combined perineal powders 23 to include cornstarch. So each 24 paper is different, okay? We</p>
<p style="text-align: right;">Page 131</p> <p>1 it's even relevant to discuss it at this 2 point. I think that we've had many -- 3 much more data since then. And that the 4 same data was available to IARC in 2010 5 and they found it not, you know, 6 compelling. 7 Q. And IARC 2010 reviewing 8 literature up to 2006 specifically dealt 9 with non-asbestiform talc, correct? 10 A. The same talc that 11 Dr. Balkwill lists in this paper. 12 Q. How do you know what talc 13 she is referring to? 14 A. Well, she just says talc 15 which is, you know, basically -- if we 16 look at the paper I'm sure we can find 17 the citations to the same papers that 18 IARC considered. 19 Q. But you've -- you've already 20 testified that when you use talc, you're 21 referring to talcum powder products; 22 whereas, IARC was specific about 23 non-asbestiform talc, correct? 24 MR. LOCKE: Objection to</p>	<p style="text-align: right;">Page 133</p> <p>1 can't lump them together. 2 BY DR. THOMPSON: 3 Q. Okay. 4 A. What was the second half of 5 the question? Because I didn't catch 6 that. 7 Q. Let's go on. Have you 8 talked to Dr. Balkwill about the opinions 9 regarding talc in this paper? 10 A. No. As I told you, I 11 haven't spoken to anybody about my 12 opinions in this case. 13 Q. Did you review this paper 14 when you were looking at the subject of 15 talc and its relationship to ovarian 16 cancer? 17 A. I did scan through this 18 paper. That's -- I'm familiar with this 19 paper anyway. But as I said, it's from 20 2001. 2001 really is like, it's like 21 ancient history in cancer biology. I 22 know that sounds crazy, but it really is. 23 Q. You would agree that our 24 plaintiffs in this case, most of which</p>

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<p>1 were using talcum powder throughout 2 decades, but certainly were using it in 3 2001, correct? 4 A. I don't know what your -- I 5 don't know your specific plaintiffs, 6 except that I know that they had ovarian 7 cancer, for which I'm very sorry. 8 Q. So when this paper came out 9 in 2001 stating that there was some 10 association between inflammation and 11 cancer risk, listing ovarian as the 12 malignancy that it applied to and talc as 13 an inflammatory stimulus and condition, 14 would that have caused anyone concern in 15 2001? 16 MR. LOCKE: Objection. 17 MS. SHARKO: Object to the 18 form. 19 THE WITNESS: Who is 20 "anyone"? 21 BY DR. THOMPSON: 22 Q. Would that have caused you 23 concern about whether talc should be used 24 by women in the genital region in 2001</p>	<p>1 reviewed all of the literature in this 2 area. 3 Q. I asked what she did. 4 A. I don't know what she did. 5 But we can look at her citations. 6 Q. Have you spoken to 7 Dr. Balkwill about her opinions in this 8 paper? 9 A. No. I said that I hadn't. 10 Q. And when was the last time 11 that you spoke to her? 12 A. The last time I saw Fran was 13 probably 2015, maybe. I don't know for 14 sure though. I saw her at a meeting. 15 Q. Are you familiar with Simone 16 Reuter? 17 A. Well, I don't know. I have 18 to see the spelling. Maybe I am and it's 19 just not pronounced correctly. 20 (Document marked for 21 identification as Exhibit 22 Neel-10.) 23 BY DR. THOMPSON: 24 Q. And this is another review</p>
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<p>1 when this paper was published? 2 A. So -- okay, if I were 3 involved in regulation in 2001, I would 4 have done exactly what I did in this 5 case, which was to review the literature 6 available at the time. And I would have 7 found it wanting and not compelling, as 8 IARC did in 2010, when they reviewed the 9 literature that it was up to 2006, which 10 obviously included this paper in 2001. 11 So I think that the fact 12 that it's stated in this paper as an 13 association, does not mean that 14 Dr. Balkwill did an extensive review of 15 the literature, as I did. 16 And, therefore, I really 17 doubt that if Fran Balkwill were sitting 18 right here, she would say otherwise. 19 Q. That's pure speculation, 20 correct? 21 A. Okay. Yes. 22 Q. You don't know what kind of 23 review she did? 24 A. Well, I do know that I</p>	<p>1 article that will be Exhibit 10. Have 2 you seen this article before? 3 A. I don't think so. But I 4 know these authors. 5 Q. Okay. And are they credible 6 researchers scientists in your opinion? 7 A. No. 8 Q. And what led you to make 9 that conclusion? 10 A. I've reviewed some papers by 11 the senior author and I find them to be 12 very poor. 13 Q. These authors are at M.D. 14 Anderson Cancer Center in Houston, 15 correct? 16 A. I don't know if they're 17 still there. But yes. This is -- 18 Q. That's where they wrote this 19 paper? 20 A. -- from 2010. 21 Q. And M.D. Anderson certainly 22 has a good reputation as a cancer center, 23 correct? 24 A. Well, I actually</p>

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<p style="text-align: right;">Page 138</p> <p>1 participated in external reviews of 2 various programs at M.D. Anderson. And I 3 find some of the scientists are good and 4 some of them are not very good. And I've 5 written that, and knowing -- we 6 participate in a review of one of the 7 departments there. So I'm pretty 8 familiar with the science at M.D. 9 Anderson. 10 It's a gigantic institution, 11 and the quality of the research varies 12 from laboratory to laboratory. 13 Q. Okay. And this article is 14 titled, from 2010, "Oxidative Stress, 15 Inflammation, and Cancer: How Are They 16 Linked?" 17 And in the abstract, the 18 authors state, "How oxidative stress 19 activates inflammatory pathways leading 20 to transformation of a normal cell to 21 tumor cell, tumor cell survival, 22 proliferation, chemo resistance, 23 radioresistance, invasion, angiogenesis, 24 and stem cell survival is the focus of</p>	<p style="text-align: right;">Page 140</p> <p>1 on the specific topic. Different things 2 are developing at different times. So 3 the genomics, for example, the genetic 4 changes occurring, I would say largely 5 defined in the beginning of 2012. 6 The evidence showing cell of 7 origin is still somewhat emerging. It 8 depends on the specific details. 9 Q. So any theory or any -- 10 scratch that. 11 Any mechanism that describes 12 oxidative stress and inflammation as 13 relevant to the pathogenesis of 14 epithelial ovarian cancer is irrelevant? 15 A. No, I didn't say that. 16 First of all, I think that you're 17 conflating several things. Oxidative 18 stress is separate from inflammation. 19 They can be linked, they can be separate. 20 We'd have to talk about each one of them 21 separately. 22 In terms of oxidative 23 stress, the oxidative stress in most 24 cases that's associated with cancer</p>
<p style="text-align: right;">Page 139</p> <p>1 this review." 2 Would you agree that those 3 events, starting with inflammatory 4 pathways leading to, are hallmarks of 5 carcinogenesis? 6 A. I think that as I said 7 before, in some cancers chronic 8 inflammation is definitely part of the 9 initiation event. 10 This paper is from 2010. 11 And it is generically talking about 12 pathways that are involved in cancer. It 13 has no specific relevance to ovarian 14 cancer. And in fact, as I said before, 15 the evidence today in 2019, which is a 16 lifetime ago from 2010 in cancer biology, 17 directly assesses this with knowledge of 18 the premalignant lesions and looking at 19 the premalignant lesions and finding no 20 inflammation. 21 Q. At what point in time can we 22 consider an article that relates to 23 ovarian cancer as relevant? 24 A. It depends on -- it depends</p>	<p style="text-align: right;">Page 141</p> <p>1 pathogenesis is coming from endogenous 2 reactive oxygen formation that's 3 catalyzed by cellular respiration through 4 mitochondria and the uncoupling reactions 5 that occur there. 6 Q. And any scientist who 7 disagrees with that is wrong? 8 A. With what? 9 Q. What you just said? 10 A. Which part? That oxidative 11 stress and inflammation are 12 intellectually linked? 13 Q. That it's coming from -- 14 catalyzed by cellular rest through 15 mitochondria -- 16 A. Respiration. 17 Q. Respiration. 18 -- and not from exogenous or 19 extrinsic factors. 20 A. It depends -- 21 MS. SHARKO: Wait, wait. 22 What is the question? 23 BY DR. THOMPSON: 24 Q. That the cancer would be</p>

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<p>1 coming from mitochondrial respiration --</p> <p>2 endogenous mitochondrial respiration and</p> <p>3 not extrinsic factors.</p> <p>4 A. It depends on the specific</p> <p>5 cancer and it depends on the specific</p> <p>6 context.</p> <p>7 For example, in the case of</p> <p>8 H pylori induced gastric cancer, the</p> <p>9 H pylori provokes inflammation, and the</p> <p>10 inflammation results in the immigration</p> <p>11 of immune cells and they may contribute</p> <p>12 to oxidative stress by producing reactive</p> <p>13 oxygen species.</p> <p>14 But in many cancers, the</p> <p>15 reactive oxygen is coming from endogenous</p> <p>16 respiration, and one of the theories for</p> <p>17 obesity and causing cancer goes through</p> <p>18 that.</p> <p>19 In the case of ovarian</p> <p>20 cancer, there may be -- there is evidence</p> <p>21 that is still emerging about whether</p> <p>22 follicular fluid has reactive oxygen</p> <p>23 species in it, and that may contribute to</p> <p>24 the incessant ovulation hypothesis.</p>	<p>1 closely linked."</p> <p>2 Do you agree or disagree</p> <p>3 with that statement?</p> <p>4 A. I agree with that for some</p> <p>5 cancers, but I don't agree with that for</p> <p>6 all cancers.</p> <p>7 So, again, to talk about</p> <p>8 cancer as an entity is even more</p> <p>9 irrelevant than to talk about epithelial</p> <p>10 ovarian cancer as a -- as an entity.</p> <p>11 It's like talking about infectious</p> <p>12 disease.</p> <p>13 Q. Okay. And in Table 2 of</p> <p>14 this article, the authors include a</p> <p>15 partial list of cancers that have been</p> <p>16 linked to reactive oxygen species. And</p> <p>17 ovarian cancer is listed, isn't it?</p> <p>18 A. We can look at the</p> <p>19 reference. I have to see what the</p> <p>20 reference is.</p> <p>21 Q. Well, I'm just asking you if</p> <p>22 it's listed in this table.</p> <p>23 A. It's listed in the table.</p> <p>24 Q. Okay. That was my question.</p>
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<p>1 Q. Okay. I didn't ask about</p> <p>2 H pylori or follicular fluid.</p> <p>3 A. Well, you asked about</p> <p>4 cancer.</p> <p>5 MS. SHARKO: You don't need</p> <p>6 to respond to that. She's going</p> <p>7 to ask you another question.</p> <p>8 BY DR. THOMPSON:</p> <p>9 Q. These authors state,</p> <p>10 "Overall, observations to date suggest</p> <p>11 that oxidative stress, chronic</p> <p>12 inflammation, and cancer are closely</p> <p>13 linked."</p> <p>14 Do you agree or disagree</p> <p>15 with that statement?</p> <p>16 A. I think that it depends on</p> <p>17 the context and that that -- a general</p> <p>18 statement like that is not necessarily</p> <p>19 correct for any individual cancer.</p> <p>20 Q. Well, the context is in a</p> <p>21 review article about cancer in general.</p> <p>22 "Overall, observations to</p> <p>23 date suggest that oxidative stress,</p> <p>24 chronic inflammation, and cancer are</p>	<p>1 In your report, you list the</p> <p>2 differences between a risk factor and a</p> <p>3 causal association, correct?</p> <p>4 A. Yes.</p> <p>5 Q. And what are those</p> <p>6 differences?</p> <p>7 A. A causal association has</p> <p>8 some biological plausibility attached to</p> <p>9 it, a mechanistic plausibility.</p> <p>10 Q. And turning to Page 16 of</p> <p>11 your report under plausibility.</p> <p>12 MS. SHARKO: You can't write</p> <p>13 on the exhibits.</p> <p>14 THE WITNESS: Oh, I can't</p> <p>15 draw? Sorry.</p> <p>16 BY DR. THOMPSON:</p> <p>17 Q. You state, "For an agent to</p> <p>18 be adjudged the cause of cancer, there</p> <p>19 must be a demonstration of a plausible</p> <p>20 biochemical mechanism."</p> <p>21 What do you mean by</p> <p>22 demonstration?</p> <p>23 A. What do I mean by</p> <p>24 demonstration?</p>

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<p>1 Q. Yes.</p> <p>2 A. Experiment, scientific, you</p> <p>3 know, proof. Evidence.</p> <p>4 Q. Doesn't that mean more than</p> <p>5 plausible?</p> <p>6 A. No.</p> <p>7 Q. Does plausible mean that</p> <p>8 there has to have been an experiment</p> <p>9 demonstrating the mechanism?</p> <p>10 A. There has to be some</p> <p>11 evidence that the mechanism is true, yes.</p> <p>12 You know, just a hypothesis is not</p> <p>13 plausibility. Not biochemical</p> <p>14 plausibility.</p> <p>15 Q. So in your opinion, the</p> <p>16 plausible mechanism has to be actually</p> <p>17 demonstrated by an experiment, correct?</p> <p>18 A. Yes.</p> <p>19 Q. Let's look at the Bradford</p> <p>20 Hill.</p> <p>21 I believe you used this</p> <p>22 reference when you were doing the</p> <p>23 Bradford Hill evaluation in your report?</p> <p>24 A. Which reference?</p>	<p>1 Bradford Hill, when originally providing</p> <p>2 his guidelines, did not require that the</p> <p>3 mechanism be demonstrated by</p> <p>4 experimentation?</p> <p>5 MS. SHARKO: Well, you</p> <p>6 didn't read that whole -- the</p> <p>7 whole section. Right?</p> <p>8 DR. THOMPSON: I read what I</p> <p>9 read.</p> <p>10 If Dr. Neel needs to read</p> <p>11 the whole section to answer my</p> <p>12 question, he can.</p> <p>13 THE WITNESS: Yeah. This</p> <p>14 was in the context -- I read the</p> <p>15 whole paper. And this was in the</p> <p>16 context of when you have a hazard</p> <p>17 ratio of like, 240 to 1, like they</p> <p>18 did for chimney sweeps, then, you</p> <p>19 know, the requirement for</p> <p>20 experiment is less.</p> <p>21 But for, you know, a series</p> <p>22 of epidemiological associations</p> <p>23 which are conflicting and weak,</p> <p>24 the biological plausibility</p>
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<p>1 Q. The Bradford Hill 1965. The</p> <p>2 original report.</p> <p>3 A. Mm-hmm.</p> <p>4 DR. THOMPSON: And I'll go</p> <p>5 ahead and mark this Exhibit 11.</p> <p>6 (Document marked for</p> <p>7 identification as Exhibit</p> <p>8 Neel-11.)</p> <p>9 BY DR. THOMPSON:</p> <p>10 Q. Let's actually look at --</p> <p>11 this will be Page 4, Page 298 of the</p> <p>12 original paper.</p> <p>13 A. Page 2. Line what?</p> <p>14 Q. 298, under plausibility.</p> <p>15 A. Yep.</p> <p>16 Q. And at least the Bradford</p> <p>17 Hill framework under plausibility states,</p> <p>18 "It will be helpful if the causation we</p> <p>19 suspect is biologically plausible. But</p> <p>20 this is a feature I am convinced we</p> <p>21 cannot demand. What is biologically</p> <p>22 plausible depends on the biological</p> <p>23 knowledge of the day."</p> <p>24 Would you agree with me that</p>	<p>1 becomes essential.</p> <p>2 And then also this paper was</p> <p>3 written in 1965 when cancer</p> <p>4 biology was developed to a far</p> <p>5 lesser extent.</p> <p>6 So I think that the general</p> <p>7 standard for a cancer biologist to</p> <p>8 accept causation would require</p> <p>9 experiments in 2019. And I state</p> <p>10 that as an editor -- a member of</p> <p>11 the editorial board of six</p> <p>12 journals, including the two most</p> <p>13 prominent cancer biology journals.</p> <p>14 I can assure you that no one</p> <p>15 would accept a manuscript for</p> <p>16 publication in a high quality</p> <p>17 journal that did not have evidence</p> <p>18 of biological plausibility</p> <p>19 supported by experiments in 2019.</p> <p>20 BY DR. THOMPSON:</p> <p>21 Q. I'm just asking you</p> <p>22 Dr. Hill's statements regarding</p> <p>23 plausibility.</p> <p>24 A. Well, I suspect Dr. Hill is</p>

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<p>1 no longer alive, but this is from 1965. 2 And I don't think we should be applying 3 1965 standards to 2019 science. 4 Q. Isn't that what you applied 5 in your report when you did the causation 6 analysis? 7 A. I applied the general 8 frame -- I applied the general framework. 9 I didn't apply the -- every conclusion in 10 Dr. Hill's paper. 11 Q. Okay. 12 A. Standards change over time. 13 Q. But looking at Bradford 14 Hill, as published in 1965, and as you 15 said, you applied in your report to some 16 degree, you would agree that the 17 mechanism does not have to be proven, 18 correct? 19 A. The mechanism does not have 20 to be proven to say what? 21 Q. To say that -- to be 22 causative, the mechanism for how the 23 agent is associated with an outcome, that 24 causative, that it doesn't have to be</p>	<p>1 think you can find a credible scientist 2 in the world -- or in the United States 3 or the world who would say otherwise. 4 That is generally accepted scientific 5 practice in 2019. 6 Q. And that's Dr. Neel's 7 standard? 8 A. No. That is generally 9 accepted scientific practice in 2019. 10 I'm sure that if -- you 11 know, if you asked any other significant 12 scientist in the United States, they 13 would agree with that statement. 14 Q. But where can I find that 15 published? 16 A. I don't -- I mean I don't 17 know if it is published. But that is 18 generally the -- that is definitely the 19 standard. 20 Q. You would agree that 21 plausible and demonstrable do not mean 22 the same thing, right? 23 A. In the context of biological 24 plausibility, yes, they do -- they do</p>
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<p>1 proven? 2 A. There has to be some 3 evidence for it. Some -- some credible 4 scientific evidence for which there is 5 none in the current case. 6 Q. Where could I find the -- 7 the standard that you apply that it has 8 to be demonstrated in an experiment for 9 something to be causal? 10 A. Where could you find that 11 standard? 12 Q. Where would I find an 13 article that says that's the standard 14 that should be used? 15 A. I'm telling you, I'm telling 16 you as a scientist who is the editor of 17 major scientific journals and a reviewer 18 for every major scientific journal, that 19 that is the accepted standard in science. 20 If you ask any major 21 scientist in the United States what is 22 the accepted standard for establishing 23 causation, they will tell you a 24 mechanism-based experiment. I don't</p>	<p>1 mean the same thing essentially. 2 They mean experimentally 3 demonstrated or experimentally supported. 4 Q. Does the Bradford Hill 5 analysis require the evidence to be 6 compelling? 7 A. I don't know what -- what 8 the Bradford Hill analysis means, whether 9 Bradford Hill -- it doesn't mean -- I 10 don't know if he uses the word 11 compelling. We can read through the 12 entire thing. 13 Again, I want to clarify, I 14 used the Bradford Hill framework to reach 15 my conclusions. I didn't necessarily use 16 every single statement in Bradford Hill's 17 paper. 18 Q. I agree. But I'm just 19 talking about the Bradford Hill 20 guidelines that you cited and applied in 21 your report. 22 A. Framework. 23 Q. Do -- does the Bradford Hill 24 framework require that the evidence be</p>

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<p>1 compelling?</p> <p>2 A. We can read through the</p> <p>3 whole thing and see if he uses the word</p> <p>4 "compelling."</p> <p>5 Q. Okay. Go ahead.</p> <p>6 A. Okay.</p> <p>7 Q. It would be under biological</p> <p>8 plausibility. That's what we're</p> <p>9 referring to.</p> <p>10 A. Well, again, as I said</p> <p>11 before, the -- this is one of the</p> <p>12 criteria. If the other criteria are</p> <p>13 weak, this becomes extremely important.</p> <p>14 And there is no strong evidence of</p> <p>15 anything else.</p> <p>16 So I don't really -- I don't</p> <p>17 know if he uses the word "compelling" in</p> <p>18 here. But in my opinion, in order to</p> <p>19 establish biological plausibility, there</p> <p>20 has to be compelling scientific evidence,</p> <p>21 yes.</p> <p>22 Q. Okay. All right. In your</p> <p>23 opinion, does a Bradford Hill analysis</p> <p>24 require the evidence to be convincing?</p>	<p>1 used the Bradford Hill analysis, as a</p> <p>2 framework.</p> <p>3 Q. And direct and plausible</p> <p>4 mean different things, right?</p> <p>5 A. Direct and plausible mean</p> <p>6 different things? They clearly mean</p> <p>7 different things, but they don't mean</p> <p>8 different things in the context of</p> <p>9 convincing scientific evidence of</p> <p>10 biological plausibility.</p> <p>11 Q. Okay. So in --</p> <p>12 A. The common use --</p> <p>13 Q. In the way that you have</p> <p>14 interpreted a causation analysis, a</p> <p>15 plausible mechanism would need to be</p> <p>16 direct evidence, correct?</p> <p>17 MS. SHARKO: Were you done</p> <p>18 with your last answer?</p> <p>19 THE WITNESS: I can answer</p> <p>20 it in the context of this</p> <p>21 question.</p> <p>22 Can you repeat the question</p> <p>23 though?</p> <p>24 BY DR. THOMPSON:</p>
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<p>1 A. Yes. Not a Bradford Hill.</p> <p>2 My analysis. I can't really comment on</p> <p>3 what Bradford Hill would see as the</p> <p>4 standard.</p> <p>5 As I said, I used the</p> <p>6 Bradford Hill framework to frame my</p> <p>7 report. I did not use Bradford Hill's</p> <p>8 personal opinion, obviously. I used my</p> <p>9 scientific opinion.</p> <p>10 Q. Okay. But I'm -- but you</p> <p>11 had referred to the Bradford Hill</p> <p>12 analysis in your report, so I'm just</p> <p>13 trying to understand how you used that</p> <p>14 analysis in --</p> <p>15 A. As a framework.</p> <p>16 Q. -- as a framework.</p> <p>17 Did the Bradford Hill</p> <p>18 analysis require that evidence be direct?</p> <p>19 A. As I said, I used the</p> <p>20 Bradford Hill -- the Bradford Hill paper</p> <p>21 as a framework to discuss the issues</p> <p>22 regarding the pathogenesis of ovarian</p> <p>23 cancer and the relationship, if any, to</p> <p>24 talc. Okay. That is the only way that I</p>	<p>1 Q. In the way that you have</p> <p>2 interpreted a causation analysis, a</p> <p>3 plausible mechanism would need to be</p> <p>4 direct evidence, correct?</p> <p>5 A. It would need to be direct</p> <p>6 experimental evidence.</p> <p>7 Q. Direct experimental</p> <p>8 evidence.</p> <p>9 A. Yes, yes.</p> <p>10 Q. And --</p> <p>11 A. And can I finish? I</p> <p>12 actually wasn't finished.</p> <p>13 Q. I'm sorry.</p> <p>14 A. Direct experimental evidence</p> <p>15 that is scientifically credible that</p> <p>16 there is a causal relationship between</p> <p>17 the agent and the disorder under</p> <p>18 question, whether it's neoplastic or not.</p> <p>19 Q. And same thing with</p> <p>20 definitive. Does the Bradford Hill</p> <p>21 framework work require that for evidence</p> <p>22 to be plausible, it should be definitive?</p> <p>23 A. Again, I'm not using -- I'm</p> <p>24 using Bradford Hill criteria as a</p>

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<p>1 framework for addressing the issues of</p> <p>2 causation here in my report.</p> <p>3 I don't know whether --</p> <p>4 whether -- what was -- what was the word?</p> <p>5 Credible?</p> <p>6 Q. We're on definitive.</p> <p>7 A. Definitive. In my</p> <p>8 professional opinion, evidence has to be</p> <p>9 definitive to attribute causation. Yes.</p> <p>10 And by definitive, I mean</p> <p>11 credible scientific data to support the</p> <p>12 plausibility claim. And there is none in</p> <p>13 this case.</p> <p>14 Q. Does the evidence under a</p> <p>15 Bradford Hill framework for the mechanism</p> <p>16 to be plausible need to be conclusive?</p> <p>17 A. Again, I'm going to say the</p> <p>18 same thing that I said before.</p> <p>19 In order to have an argument</p> <p>20 in favor of biological plausibility, the</p> <p>21 data has to be conclusive and convincing.</p> <p>22 Bad data are of no use. Bad</p> <p>23 experiments are of no use. Sometimes</p> <p>24 they are of less than no use, because</p>	<p>1 not a risk factor for epithelial ovarian</p> <p>2 cancer?</p> <p>3 A. That states it's not?</p> <p>4 Q. Yes. An article that says</p> <p>5 we have reviewed the evidence and talcum</p> <p>6 powder is not a risk factor for</p> <p>7 epithelial --</p> <p>8 A. I think that it's not an</p> <p>9 established risk factor. There is no --</p> <p>10 there is no agreement on talc being a</p> <p>11 risk factor for ovarian cancer. So it's</p> <p>12 not an established risk factor.</p> <p>13 I think, you know, we can go</p> <p>14 to my report, but I'm pretty sure</p> <p>15 statements were made to that effect by</p> <p>16 IARC, possible. They said the data</p> <p>17 aren't compelling. So yes.</p> <p>18 Q. Is it not what -- is it that</p> <p>19 it's not well established, or is it not a</p> <p>20 risk factor?</p> <p>21 A. There is no compelling</p> <p>22 evidence. There is no credible</p> <p>23 scientific evidence that it's a risk</p> <p>24 factor. There is no consistent evidence</p>
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<p>1 they are misleading.</p> <p>2 Q. And this is the last one.</p> <p>3 A. Sure.</p> <p>4 Q. And I just want to</p> <p>5 understand words that you have used in</p> <p>6 your report.</p> <p>7 A. Mm-hmm.</p> <p>8 Q. Using a Bradford Hill</p> <p>9 framework, does evidence for plausibility</p> <p>10 need to be strong?</p> <p>11 A. In my opinion, to attribute</p> <p>12 causation of any agent to the initiation</p> <p>13 of any malignancy, the evidence has to be</p> <p>14 strong, convincing, and definitive, yes.</p> <p>15 Q. Okay. Let's move on to</p> <p>16 another topic.</p> <p>17 Is it your opinion that the</p> <p>18 genital use of talcum powder is not a</p> <p>19 risk factor for epithelial ovarian</p> <p>20 cancer?</p> <p>21 A. Yes. That's my opinion.</p> <p>22 Q. And can you cite any</p> <p>23 literature that explicitly states that</p> <p>24 talcum powder use in the perineal area is</p>	<p>1 that it's a risk factor. There is no</p> <p>2 agreed-upon definition that it's a risk</p> <p>3 factor.</p> <p>4 Q. Is it a possible risk</p> <p>5 factor?</p> <p>6 A. I think that, you know, IARC</p> <p>7 considers it a possible carcinogen as of</p> <p>8 2010.</p> <p>9 I think the evidence that's</p> <p>10 developed 2010 makes it less likely that</p> <p>11 it's even possible.</p> <p>12 Q. Could credible scientists</p> <p>13 look at the evidence and determine that</p> <p>14 the genital use of talcum powder is a</p> <p>15 risk factor for ovarian cancer?</p> <p>16 A. No, not in my opinion. I</p> <p>17 don't think so.</p> <p>18 Q. So would those doctors or</p> <p>19 scientists, looking at the evidence and</p> <p>20 reaching those opinions be uninformed?</p> <p>21 A. I can't comment on the basis</p> <p>22 of their opinions without seeing their</p> <p>23 opinions.</p> <p>24 Q. But at least in your</p>

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<p>1 opinion, they could not credibly come to 2 that conclusion? 3 A. Not based on the evidence 4 that I reviewed and considered in my 5 report, no. 6 Q. Okay. And you have a 7 section in your report on risk factors 8 for ovarian cancer in which you discuss 9 some of them, beginning on Page 12. 10 You only cite one article, 11 and that is the Reid paper. And we'll 12 mark that as 12. 13 (Document marked for 14 identification as Exhibit 15 Neel-12.) 16 MS. SHARKO: Where -- where 17 are you talking about? 18 THE WITNESS: It's on the 19 next page. 20 MS. SHARKO: So we're not on 21 Page 12. 22 DR. THOMPSON: Well, it 23 begins multiple factors likely 24 contribute to ovarian cancer, on</p>	<p>1 Do they state that? 2 A. Actually I think you're 3 misstating their conclusions. I'll read 4 their conclusions. 5 Q. Well, I -- only -- 6 A. "However a" -- 7 Q. I -- 8 A. You asked me a question. 9 Can I answer it? 10 Q. I -- I am reading, did I 11 read this correctly: "Other possible 12 risk factors include environmental and 13 lifestyle factors such as asbestos and 14 talc powder exposures and cigarette 15 smoking." 16 Did I read that correctly? 17 A. Where are you reading at? 18 Q. In the abstract? 19 MS. SHARKO: So wait a 20 minute. You asked him a question. 21 He tried to answer it. You 22 interrupted him. 23 DR. THOMPSON: Well, I asked 24 him --</p>
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<p>1 Page 12. 2 THE WITNESS: I got it. 3 BY DR. THOMPSON: 4 Q. This is the paper that you 5 refer to in your report as really the 6 only paper that you -- that you cite on 7 risk factors for ovarian cancer, correct? 8 A. Yes, because it's the most 9 recent comprehensive review on the 10 subject. 11 Q. And the authors are 12 epidemiologists, correct? 13 A. Yes. 14 Q. They are not physicians, 15 correct? 16 A. No, but Tom Sellers is an 17 expert in ovarian cancer epidemiology. I 18 know him personally. He is the director 19 of Moffitt Cancer Center in Tampa. 20 Q. And the authors actually 21 state that "other possible risk factors 22 include environmental and lifestyle 23 factors such as asbestos and talc powder 24 exposures."</p>	<p>1 MS. SHARKO: He gets to 2 answer the question or you 3 withdraw it. 4 DR. THOMPSON: I asked him 5 if they stated that. He did not 6 need to tell me about something 7 else when I was asking the 8 question, was that stated by the 9 authors. 10 MS. SHARKO: You don't need 11 to raise your voice. He's trying 12 to answer your question. 13 DR. THOMPSON: Okay. All 14 right. 15 Let's just start all over. 16 I think the record will speak for 17 itself. 18 BY DR. THOMPSON: 19 Q. Dr. Neel, do the authors 20 state -- 21 A. Where are you quoting from 22 first? 23 Q. In the abstract, the next to 24 the last sentence.</p>

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<p>1 Do the authors state: 2 "Other possible risk factors include 3 environmental and lifestyle factors such 4 as asbestos and talc powder exposures and 5 cigarette smoking"? 6 A. Yes, that's what it says 7 there. But it's out -- you are reading 8 it out of context. 9 Q. I just ask if they say that. 10 But you didn't include in 11 your report where you use this article, 12 that the authors stated that possible 13 risk factors include environmental and 14 lifestyle factors such as asbestos and 15 talc exposure, did you? 16 A. The entire -- my entire 17 report was focused around talc. The 18 other -- what I cited in this context, in 19 my report, were the other claimed risk 20 factors in ovarian cancer. I was 21 discussing the other risk factors. The 22 rest of the report concerns my views on 23 talc as a risk factor. So there was no 24 reason to cite it here. The entire</p>	<p>1 So I -- I don't really think 2 there's any conflict here. 3 And you stated out of 4 context what's in the abstract. 5 And -- and again, a lot of 6 times when authors are setting up 7 a paper, they will post, you know, 8 all possibilities that are in the 9 literature and then they will 10 reach their own conclusions. 11 So for you to lift that out 12 of context is really not accurate 13 in my opinion. 14 BY DR. THOMPSON: 15 Q. And did you review any other 16 articles that discussed risk factors for 17 ovarian cancer other than the Reid paper? 18 A. Yes, I -- I read multiple 19 papers on ovarian cancer pathogenesis, 20 but I can't tell you right now. 21 I cited this one, because 22 this is the most up-to-date comprehensive 23 view of ovarian cancer risk factors. 24 And my goal in my report was</p>
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<p>1 report concerns that. 2 But again, I must insist 3 that you are taking out of context 4 Dr. Reid -- Dr. Sellers' conclusions. I 5 found Dr. Sellers' conclusions to be 6 quite continent with my own based on the 7 actual section -- 8 Q. And you'll have another 9 opportunity if Ms. Sharko wants to come 10 back. 11 MS. SHARKO: Wait. 12 Were you done with your 13 answer? 14 THE WITNESS: I was almost 15 done. Okay. 16 MS. SHARKO: Finish your 17 answer. 18 THE WITNESS: If one goes to 19 Page 18 of the same paper that 20 you're citing, and actually reads 21 the section on asbestos and talcum 22 powder, you will see that his 23 opinions and mine are almost 24 identical.</p>	<p>1 not to write a review of all the risk 2 factors for ovarian cancer. The goal of 3 my report and the topic which I'm here to 4 testify here today on, is the role of 5 talc and Johnson & Johnson products in -- 6 and the possible role of talc and Johnson 7 & Johnson products in ovarian cancer 8 pathogenesis. 9 The entirety of my report 10 focuses primarily on that issue. This 11 section on other risk factors was in the 12 context of background of other issues 13 concerning ovarian cancer. Not whether 14 or not talc was involved. 15 Q. Okay. Let's just look at 16 some other articles relating to risk 17 factors -- 18 A. Sure. 19 Q. -- and see if there are 20 scientists that disagree with that 21 opinion. 22 A. Well, I just want to clarify 23 again. Dr. Sellers does not -- 24 MS. SHARKO: Wait, wait,</p>

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<p>1 wait.</p> <p>2 THE WITNESS: -- disagree</p> <p>3 with my opinion.</p> <p>4 BY DR. THOMPSON:</p> <p>5 Q. I -- we have moved on from</p> <p>6 Dr. Sellers.</p> <p>7 A. Okay. Well, you said other</p> <p>8 scientists so I just want to get --</p> <p>9 Q. Well, I'm about to show</p> <p>10 you --</p> <p>11 A. Okay.</p> <p>12 MS. SHARKO: She's going to</p> <p>13 ask you a new question.</p> <p>14 BY DR. THOMPSON:</p> <p>15 Q. I'm going to ask you a new</p> <p>16 question.</p> <p>17 MS. SHARKO: That was just a</p> <p>18 speech.</p> <p>19 THE WITNESS: Okay.</p> <p>20 MS. SHARKO: Wait for a</p> <p>21 question.</p> <p>22 THE WITNESS: I thought that</p> <p>23 was -- okay.</p> <p>24 MS. SHARKO: Okay.</p>	<p>1 these authors.</p> <p>2 Q. Okay. That wasn't the</p> <p>3 question.</p> <p>4 Under lifestyle factors,</p> <p>5 these authors state, "A lot of work has</p> <p>6 been done to clarify the risk reduction</p> <p>7 of various lifestyle approaches, such as</p> <p>8 alcohol, obesity, cigarette smoking and</p> <p>9 talc use. Some of these are subtype</p> <p>10 specific, such as endometriosis,</p> <p>11 cigarette smoking and obesity, while</p> <p>12 others are general risk factors.</p> <p>13 "Use of talc in the genital</p> <p>14 area has consistently been shown to</p> <p>15 increase the risk of ovarian cancer and,</p> <p>16 therefore, is not recommended."</p> <p>17 Did I read that correctly?</p> <p>18 A. Yes, you did.</p> <p>19 Q. So these authors at least do</p> <p>20 consider talc use a risk factor, correct?</p> <p>21 A. Apparently.</p> <p>22 Q. And -- and consider it a</p> <p>23 general risk factor, even understanding</p> <p>24 that there are some risk factors that are</p>
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<p>1 There is exhibit -- what is</p> <p>2 that, 13?</p> <p>3 (Document marked for</p> <p>4 identification as Exhibit</p> <p>5 Neel-13.)</p> <p>6 BY DR. THOMPSON:</p> <p>7 Q. And I'm handing you</p> <p>8 Exhibit 13, which comes from a textbook</p> <p>9 titled "Cancer Prevention and Screening."</p> <p>10 And if you will turn to</p> <p>11 Page 337.</p> <p>12 MS. SHARKO: Do you have the</p> <p>13 year on this?</p> <p>14 THE WITNESS: 2019. It's on</p> <p>15 the bottom of the first page.</p> <p>16 BY DR. THOMPSON:</p> <p>17 Q. So you would agree that --</p> <p>18 A. What page please?</p> <p>19 Q. 337.</p> <p>20 A. Okay.</p> <p>21 Q. So you'll agree that this is</p> <p>22 an up-to-date chapter in a textbook as</p> <p>23 well?</p> <p>24 A. Yes, but I've never heard of</p>	<p>1 subtype specific, correct?</p> <p>2 A. Well, I think these authors</p> <p>3 have no knowledge of modern cancer</p> <p>4 biology, because it's not possible to</p> <p>5 cause the same genetic defects with a</p> <p>6 different agent that works by different</p> <p>7 mechanisms.</p> <p>8 Q. So the authors of this paper</p> <p>9 in your opinion are wrong?</p> <p>10 A. Yes, in my opinion.</p> <p>11 I should also -- can I just</p> <p>12 say one other thing about this?</p> <p>13 Q. Yes.</p> <p>14 A. It's notable that they cite</p> <p>15 references for alcohol, obesity and</p> <p>16 cigarette smoking, but they don't cite</p> <p>17 any references for talc use. So I can't</p> <p>18 respond to --</p> <p>19 Q. And there's no -- there's no</p> <p>20 question pending on the table.</p> <p>21 MS. SHARKO: Let him finish.</p> <p>22 Let him finish.</p> <p>23 MS. O'DELL: There's no</p> <p>24 question --</p>

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<p style="text-align: right;">Page 174</p> <p>1 DR. THOMPSON: There's no 2 question. 3 THE WITNESS: I didn't 4 finish my answer. 5 MS. O'DELL: This is not his 6 opportunity just to speak without 7 a question. There is no question. 8 MS. SHARKO: He was 9 answering the question. 10 DR. THOMPSON: He was not 11 answering my question. 12 MS. SHARKO: That's your 13 opinion, because you don't like 14 it. Dr. Neel, finish your answer. 15 BY DR. THOMPSON: 16 Q. Exhibit -- Exhibit 14 -- 17 MS. SHARKO: Stop. Dr. 18 Neel, finish your answer. 19 BY DR. THOMPSON: 20 Q. Are you finished with your 21 question, Dr. Neel? 22 A. No, I was saying -- 23 Q. I mean your answer. 24 A. -- in reading the piece --</p>	<p style="text-align: right;">Page 176</p> <p>1 risk factors, but I didn't cite one 2 article about talc, which is the issue. 3 Q. Dr. Neel, if you would try 4 as best you can to answer my question. 5 A. I am answering your 6 question. 7 Q. And my question was just did 8 you cite one article. And the answer 9 would be yes. 10 I just handed you a paper -- 11 MR. LOCKE: Objection. 12 MS. SHARKO: You don't -- 13 you don't need to respond to that 14 speech. Let's move on to the next 15 exhibit. 16 DR. THOMPSON: I don't think 17 I had a question. 18 (Document marked for 19 identification as Exhibit 20 Neel-14.) 21 BY DR. THOMPSON: 22 Q. The next article is from 23 2012, "Ovarian Cancer Etiology, Risk 24 Factors, and Epidemiology."</p>
<p style="text-align: right;">Page 175</p> <p>1 the part that you mentioned, it's notable 2 that they don't reference anything for 3 their statement on talc use. It would be 4 much more helpful if we could see what 5 evidence they want to adduce to make 6 their claim. 7 I provided very substantial 8 evidence in support of my opinions. And 9 I've also been able to discuss them. 10 This is, you know, an 11 isolated statement if a textbook that, 12 you know, probably hasn't undergone 13 scientific review. 14 Q. Well, risk factors, you 15 cited one article. We'll make that 16 clear. 17 MS. SHARKO: Well, wait. 18 No, wait a minute. You don't just 19 get to lob out comments. 20 BY DR. THOMPSON: 21 Q. Did you cite one article in 22 your risk factor discussion in your 23 paper? 24 A. I cited one article about</p>	<p style="text-align: right;">Page 177</p> <p>1 And these authors, turning 2 to Page 6, have a chart listing risk 3 factors for epithelial ovarian cancer. 4 If you'll turn to that, it's 5 on Page 6. 6 A. Yeah I have it. 7 MS. SHARKO: And this is 8 Exhibit 14 for the record. 9 DR. THOMPSON: Exhibit 14. 10 MS. SHARKO: Thank you. 11 BY DR. THOMPSON: 12 Q. And at least these authors, 13 list under inflammatory risk factors that 14 increase the risk for ovarian cancer, 15 perineal talc use, endometriosis, and 16 pelvic inflammatory disease. 17 Would you agree that these 18 authors list talc -- perineal talc 19 exposure as a risk factor? 20 A. They do. But this is 21 completely non-consummate with modern 22 research. 23 Q. I'm just asking you if the 24 authors list it.</p>

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<p>1 A. Yes, they --</p> <p>2 Q. Okay. And so these</p> <p>3 scientists who do feel -- are of the</p> <p>4 opinion that it's a risk factor are</p> <p>5 wrong?</p> <p>6 A. I don't know that they're</p> <p>7 scientists. I mean, they --</p> <p>8 Q. They're doctors. These</p> <p>9 doctors --</p> <p>10 A. There's a big difference</p> <p>11 between a doctor and a scientist. Since</p> <p>12 I have both degrees, I can state that to</p> <p>13 a very strong degree of confidence.</p> <p>14 Q. Are you saying that someone</p> <p>15 has to have two degrees to --</p> <p>16 A. No, but I'm saying that I'm</p> <p>17 very familiar with the difference in the</p> <p>18 training of the average physician and the</p> <p>19 average scientist and their ability to</p> <p>20 evaluate scientific data, and they're not</p> <p>21 the same.</p> <p>22 Q. The next one --</p> <p>23 A. There are definitely --</p> <p>24 Can I finish? There are</p>	<p>1 to any particular agent's ability to</p> <p>2 cause any kind of cancer.</p> <p>3 We know a lot -- and by the</p> <p>4 way, again, you're citing papers from</p> <p>5 2012. That's a lifetime ago in cancer</p> <p>6 biology, and specifically in ovarian</p> <p>7 cancer pathogenesis. We know much more</p> <p>8 about the cell and molecular biology of</p> <p>9 ovarian cancer today than we did then.</p> <p>10 And the fact that they put</p> <p>11 endometriosis in here is exemplary of</p> <p>12 that, because we know that endometriosis</p> <p>13 is a risk factor only insofar as the</p> <p>14 cancer is probably coming from the</p> <p>15 endometrial cells.</p> <p>16 Q. And let's turn --</p> <p>17 A. It's a cell of origin issue.</p> <p>18 It's not a carcinogenesis issue.</p> <p>19 Q. The next -- the next paper</p> <p>20 that I'm going to give you is titled</p> <p>21 "Risk Factors For Ovarian Carcinoma."</p> <p>22 (Document marked for</p> <p>23 identification as Exhibit</p> <p>24 Neel-15.)</p>
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<p>1 definitely physicians who are eminently</p> <p>2 qualified to evaluate scientific data.</p> <p>3 But the average practicing physician is</p> <p>4 not able to evaluate modern molecular</p> <p>5 data like the molecular biologist or</p> <p>6 cancer biologist. They're different</p> <p>7 disciplines.</p> <p>8 Q. If an M.D., gynecologic</p> <p>9 oncologist, who is familiar with the</p> <p>10 literature in the field gives an opinion</p> <p>11 that talcum powder use in the genital</p> <p>12 area can cause or contribute to ovarian</p> <p>13 cancer, are they wrong?</p> <p>14 A. Possibly. In my opinion</p> <p>15 they're wrong, because I've reviewed the</p> <p>16 literature comprehensively including the</p> <p>17 molecular literature, which they are</p> <p>18 probably not capable of evaluating, and</p> <p>19 they're not capable -- the average</p> <p>20 gynecologist oncologist is definitely not</p> <p>21 capable of evaluating the modern</p> <p>22 molecular data, such as mutational</p> <p>23 signatures and other more modern and</p> <p>24 comprehensive analyses that would speak</p>	<p>1 BY DR. THOMPSON:</p> <p>2 Q. And this was published in</p> <p>3 2018, correct?</p> <p>4 A. Mm-hmm.</p> <p>5 Q. If you'll turn to Page 4.</p> <p>6 MS. SHARKO: So for the</p> <p>7 record, this is Exhibit 15.</p> <p>8 DR. THOMPSON: I'm sorry.</p> <p>9 Exhibit 15.</p> <p>10 MS. SHARKO: Okay. Thank</p> <p>11 you.</p> <p>12 DR. THOMPSON: I'll try to</p> <p>13 be better about that.</p> <p>14 BY DR. THOMPSON:</p> <p>15 Q. This article titled "Risk</p> <p>16 Factors For Ovarian Cancer," if you'll</p> <p>17 turn to Page 4. There's a chart with</p> <p>18 risk factors.</p> <p>19 And this particular paper</p> <p>20 does divide the risk factors up by</p> <p>21 subtype, correct?</p> <p>22 A. Yes.</p> <p>23 MS. SHARKO: You are allowed</p> <p>24 to read the paper.</p>

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<p>1 THE WITNESS: I'm looking at 2 it, yeah. 3 MS. SHARKO: Okay. 4 THE WITNESS: Mm-hmm. 5 BY DR. THOMPSON: 6 Q. And the heading for Table 1 7 is "Summary of Putative Cells of Origin 8 and Identified Risk Factors For Specific 9 Ovarian Cancer Histologic Subtypes," 10 correct? 11 A. Yes. 12 Q. And so these authors at 13 least considered the different subtypes 14 when they were trying to classify the 15 risk factors, correct? 16 A. Yes. 17 Q. And if you'll look in this 18 chart under the heading Lifestyle Risk 19 Factors, "Genital powder use is included 20 under subtype all serous and subtype 21 endometrioid and subtype clear cell." 22 A. Mm-hmm. 23 Q. Do you agree that authors 24 considered that a risk factor for those</p>	<p>1 Looking at the -- and it was 2 published in 2018? 3 A. Mm-hmm. 4 Q. Looking at the end of the 5 paper, page -- I don't see the page. But 6 at the very end before, in -- in 7 summary -- 8 A. In the discussion? 9 Q. In -- in discussion, 10 conclusions. It states, "In particular, 11 talc powder use" -- 12 A. I'm sorry, I can't see where 13 we are. 14 Q. They -- 15 A. Oh, I see. Okay. I got it. 16 Q. In the last -- next to the 17 last paragraph. 18 "In particular, talc powder 19 use is highly prevalent in the African 20 American community and has been found to 21 be associated with increased risk of 22 ovarian cancer in this and other studies. 23 Indeed, regression models excluding talc 24 use overestimated the associations in our</p>
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<p>1 three subtypes? 2 A. Yes. 3 Q. Are these authors wrong? 4 A. Yes. And the reason they 5 are wrong is because, if you look at the 6 mutational signature, the type of 7 molecular causation of clear cell and 8 endometrioid cancer, it's completely 9 different than the molecular basis for 10 serous ovarian cancer. 11 One of them is caused by 12 chromosome abnormalities in copy number 13 variations, and the other is caused by 14 point mutations in pathways that I've 15 spent my entire career studying. 16 (Document marked for 17 identification as Exhibit 18 Neel-16.) 19 BY DR. THOMPSON: 20 Q. Next, Exhibit 16. 21 This is another paper that 22 discusses risk factors. It's part of the 23 African American cancer epidemiology 24 study that's published numerous articles.</p>	<p>1 analysis." 2 Do you agree that these 3 authors consider talc use to result in 4 increased risk of ovarian cancer in 5 African American population? 6 A. This is yet another of many 7 case-control studies which, you know, 8 claim to see an association. But they 9 are subject to the same type of recall 10 bias and other classification bias that 11 is prone to be found in case-control 12 studies. 13 The cohort studies don't 14 show this. And they are much more 15 reliable in my opinion. 16 That -- you know, so yes, 17 they say it, but that doesn't make it 18 true. 19 Q. So these authors are wrong 20 to consider talc use a risk factor for 21 ovarian cancer? 22 A. I don't think they've done a 23 complete analysis of the literature and 24 they are probably not capable of</p>

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<p>1 evaluating the molecular issues. 2 (Document marked for 3 identification as Exhibit 4 Neel-17.) 5 BY DR. THOMPSON: 6 Q. The next article is marked 7 Exhibit 17. It's a patient by Wu and her 8 colleagues. 9 MS. SHARKO: It's a paper. 10 DR. THOMPSON: What did I 11 say? 12 MS. SHARKO: Patient. 13 DR. THOMPSON: Sorry. Oh 14 boy. 15 BY DR. THOMPSON: 16 Q. It's a paper. 17 MS. SHARKO: It's almost 18 like a patient. 19 BY DR. THOMPSON: 20 Q. Let's -- let's ask that 21 question over again. 22 Exhibit 17 is a paper by 23 Dr. Wu that discusses the nongenetic risk 24 factors for ovarian cancer, correct?</p>	<p>1 to be a confirmed nongenetic risk factor 2 for ovarian cancer? 3 A. They apparently do. 4 Q. And are these authors wrong 5 as well? 6 A. Yes. And I -- I -- 7 Q. You didn't hesitate with 8 that opinion, did you? 9 A. No. Because again, if 10 you -- if you -- you're pulling out 11 individual case-control studies. And we 12 already know that 60 percent of the 13 case-control -- 67 percent of the 14 case-control studies reach one 15 conclusion, 33 percent reach the other 16 conclusion, and all the cohort studies 17 are negative. 18 That is why if you read a 19 review like Dr. Sellers' review, which is 20 a comprehensive review of the recent 21 literature concerning risk factors, you 22 will find an opinion very similar to 23 mine, which is that there is no 24 compelling evidence that talc was a</p>
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<p>1 A. Mm-hmm. 2 Q. And under the discussion 3 section of this paper, the authors state 4 that, first paragraph, "With the high 5 mortality" -- 6 A. Where -- I'm sorry, I have 7 to find it. 8 Q. Under discussion, first 9 paragraph. Page 1098. 10 "With the high mortality and 11 the lack of effective early screening for 12 ovarian cancer, better understanding of 13 preventive risk factors is a priority. 14 The primary motivation for this analysis 15 was to determine whether the six 16 confirmed nongenetic risk factors for 17 IEOC (parity, use of oral contraceptives, 18 tubal ligation, endometriosis, first 19 degree family history of ovarian cancer, 20 and use of genital talc in non-Hispanic 21 whites are also risk factors in Hispanics 22 and African Americans)." 23 Do you agree that these 24 authors believe the use of genital talc</p>	<p>1 causal -- is a cause of ovarian cancer. 2 And that's the basis of my opinion. 3 This is an -- this is a 4 single paper of a case-control study and, 5 you know, that's not as strong as 6 considering the entire body of the 7 evidence as I've done in my report. 8 Q. But doctors and scientists 9 that have a different opinion as you've 10 stated are wrong, correct? 11 MS. SHARKO: Object to the 12 form of the question. 13 THE WITNESS: In -- in each 14 individual case, I'm happy to tell 15 you whether I think they are wrong 16 or not. Okay. 17 Since I haven't met every 18 doctor and scientist who may have 19 a particular opinion, it would be 20 inappropriate for me to say that 21 all doctors and scientists who 22 have a different opinion are 23 wrong. 24 If someone comes up with</p>

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<p>1 some evidence that is convincing, 2 I will change my opinion. Right 3 now, all of the available evidence 4 suggests that there is no 5 association between genital talc 6 and ovarian cancer. And some of 7 their evidence says that there 8 isn't. 9 So there is no evidence to 10 support the case that genital talc 11 application causes ovarian cancer 12 in my scientific opinion. 13 BY DR. THOMPSON: 14 Q. Where is the evidence that 15 there isn't? 16 A. Where is the evidence that 17 there isn't? 18 Q. I think I asked you that 19 before and you could not cite to an 20 article that said it is not a risk 21 factor. 22 A. I -- 23 Q. So I would like for you to, 24 if you do have one, I would like to know</p>	<p>1 talc is not a risk factor for ovarian 2 cancer. And I said that was a risk 3 factor question. 4 If you ask me is there any 5 evidence that genital talc causes ovarian 6 cancer, there are several papers which 7 argue against that and I'm happy to cite 8 those. 9 Q. My question was risk 10 factors, so... 11 A. Okay. But you didn't ask 12 that question right before. So I was 13 answering it -- you know, you changed 14 your question, which is why it's a 15 different answer. 16 If you ask me the second 17 question I'd be happy to tell you. 18 Q. Okay. So just to be clear, 19 the answer to the question is, is there a 20 paper that explicitly states that talcum 21 powder is not a risk factor of ovarian 22 cancer, you don't have one to point to? 23 A. There are -- there are many 24 papers that review the literature --</p>
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<p>1 what -- 2 A. Oh. So -- 3 MS. SHARKO: Object. Object 4 to the form of the question. 5 Lacks foundation. Misstates his 6 testimony and apparently asked and 7 answered since you said you asked 8 it before. 9 DR. THOMPSON: Well, he had 10 a different answer. I wanted to 11 clarify it. 12 MS. SHARKO: I don't think 13 so. 14 BY DR. THOMPSON: 15 Q. Dr. -- Dr. Neel, do you 16 have -- just so I am clear. 17 Do you have an article that 18 you can point to that explicitly states 19 that talcum powder is not a risk factor 20 for ovarian cancer? 21 A. So that was a different 22 question than you just asked before. 23 The -- the question you asked before is 24 do I have a paper that says that genital</p>	<p>1 Q. I need a yes or no -- 2 A. You misstate -- 3 Q. -- question. 4 MS. SHARKO: No, no, no. 5 Wait. Timeout. 6 THE WITNESS: You asked -- 7 DR. THOMPSON: Well, he is 8 answering all kinds of questions 9 that are not what I'm asking. 10 MS. SHARKO: Well, I 11 disagree. But you've asked your 12 question. He's entitled to answer 13 it. If you want to withdraw your 14 question so be it. 15 But you can't interrupt him 16 because you don't -- 17 DR. THOMPSON: No, I want an 18 answer to my question. 19 MS. SHARKO: -- you don't 20 like his answer. 21 DR. THOMPSON: Okay. Let's 22 go back and see what the question 23 and answer were. 24 BY DR. THOMPSON:</p>

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<p>1 Q. Just to be clear, is there a 2 paper that explicitly states that talcum 3 powder is not a risk factor of ovarian 4 cancer? You don't have one to point to. 5 And his answer, is there are 6 many papers -- 7 A. You didn't let me finish. 8 Would you like me to finish? 9 Q. Okay. Well, the question 10 though was point me to a paper that 11 explicitly states that talcum powder is 12 not a risk factor for ovarian cancer. 13 A. Scientists don't generally 14 speak in that language. What they would 15 say is very similar to what Dr. Sellers 16 said, and which most of the review 17 articles about this topic say and what I 18 say. Which is there is no credible 19 scientific evidence that. 20 That is how scientists 21 speak. We have a language that we use, 22 just like lawyers have a language that 23 lawyers use. 24 And in scientific credence</p>	<p>1 BY DR. THOMPSON: 2 Q. Can you point me -- 3 MS. SHARKO: No. You asked 4 him that question already. 5 DR. THOMPSON: But I still 6 haven't got an answer. I'm going 7 to try one more time. 8 BY DR. THOMPSON: 9 Q. Can you point me to an 10 article that explicitly states that 11 talcum powder is not a risk factor for 12 ovarian cancer? 13 MS. SHARKO: Objection. 14 Asked and answered. 15 You may not like the answer, 16 but you got an answer. 17 DR. THOMPSON: Okay. The 18 record will speak for itself that 19 there is not an answer. 20 MS. O'DELL: It was asked 21 but never answered. He didn't 22 answer the question. 23 MS. SHARKO: Okay. I 24 thought -- I thought your side</p>
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<p>1 saying that -- in scientific language, 2 saying that there's no credible 3 scientific evidence is the way we would 4 state the -- the conclusion. And that's 5 how I'm stating it. That's very similar 6 to how Dr. Sellers concluded it. And 7 I -- I think that's the essence of my 8 statement. 9 Q. So your answer would be 10 you're not able to answer that question? 11 MR. LOCKE: Objection. 12 THE WITNESS: No, my answer 13 is exactly what I said. 14 BY DR. THOMPSON: 15 Q. Okay. We'll -- we'll move 16 on. 17 But I don't believe I got 18 the answer to the question: Can you 19 point me to an article that states that 20 talcum powder is not a risk factor for 21 ovarian cancer? 22 MS. SHARKO: All right. 23 That's not a question. That's an 24 editorial comment.</p>	<p>1 said the rule was that only one 2 lawyer can talk. 3 MS. O'DELL: I think the 4 evidence will show, the record 5 will show over depositions that 6 you weren't defending, Susan, you 7 had plenty to say, so I don't know 8 that I would raise that. 9 DR. THOMPSON: Including 10 last week. 11 MS. SHARKO: So the rules 12 are that one lawyer gets to 13 question the witness. So let's -- 14 MS. O'DELL: I'm not 15 questioning the witness. But I'm 16 free to speak and I will speak. 17 MS. SHARKO: You know what? 18 It seems like maybe we should just 19 take a lunch break and let 20 everybody simmer down. 21 DR. THOMPSON: I only 22 have -- I don't need a lunch 23 break. 24 MR. TISI: I'm going to tell</p>

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<p>1 you, can I have that section? 2 MS. SHARKO: So now we have 3 a third plaintiff's lawyer 4 talking? 5 MR. TISI: No, no, no. 6 We're off -- we're not talking 7 about this. 8 Can I have that clipped, 9 Ms. Sharko's comment so I can use 10 it in other depositions going 11 forward? Please, thank you. You 12 can send me that. 13 Because I expect we're going 14 to need it going forward, given 15 her behavior in the past. 16 Thank you. 17 DR. THOMPSON: Okay. 18 MS. SHARKO: You know, 19 Mr. Tisi, behave yourself. 20 DR. THOMPSON: I want -- I 21 want to move on. 22 MR. TISI: I -- I don't need 23 to be schooled by you. 24 BY DR. THOMPSON:</p>	<p>1 unclear. 2 Q. What -- how do you define a 3 carcinogen? 4 A. A carcinogen? A carcinogen 5 is an agent that causes cancer. 6 Q. And that would include 7 initiation? 8 A. Mm-hmm. 9 Q. And promotion? 10 A. Probably -- so there's a 11 difference between health scientists and 12 experimental carcinogenecist would define 13 a carcinogen and how the public would use 14 the word carcinogen. 15 In the common parlance, a 16 promotor, a tumor promoter would probably 17 be considered a carcinogen. But in 18 scientific language a carcinogen is just 19 the initiating event. 20 Q. But you'll agree that in 21 some context at least, scientists refer 22 to a carcinogen in each of those phases? 23 A. Yes. Mm-hmm, yes. 24 Q. And is it -- is that</p>
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<p>1 Q. Is it -- is it your 2 opinion -- 3 MS. SHARKO: Yeah, because 4 you don't listen. 5 MR. TISI: That's because -- 6 that's because I wouldn't listen 7 to somebody who tries to school 8 me. 9 DR. THOMPSON: I really 10 don't want to waste my time, so... 11 BY DR. THOMPSON: 12 Q. Is it your -- Dr. Neel, is 13 it your opinion that asbestos is not a 14 risk factor for ovarian cancer? 15 A. I don't have an opinion on 16 asbestos in ovarian cancer. I haven't 17 really given enough study to -- 18 Q. Okay. So you don't have an 19 opinion one way or the other as to 20 whether asbestos -- 21 A. Not -- not a strong opinion, 22 no. 23 Q. Okay. Any opinion? 24 A. I think the evidence is</p>	<p>1 sometimes referred to as a complete 2 carcinogen? 3 A. That's a kind of old term, 4 but yes. 5 Q. I'm old. 6 MS. SHARKO: Do you want 7 that on the record? 8 DR. THOMPSON: What the hey. 9 MS. SHARKO: You are not 10 old, Margaret. 11 DR. THOMPSON: Thank you, 12 Susan. That's the nicest thing 13 you've said today. 14 MS. SHARKO: Chris will 15 order that page too. 16 MR. TISI: I was -- I was 17 going to say. I was going to -- I 18 wouldn't qualify it by today. I'd 19 make it a year, but go ahead. 20 BY DR. THOMPSON: 21 Q. So let's go to Page 14 of 22 your report -- 23 A. Do you have a long question? 24 Because if not, I'm going to have to take</p>

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<p>1 a break. That coffee is having its 2 effect. 3 Q. I'm fine breaking for lunch 4 or -- 5 A. If it's a short question I 6 can answer it. 7 MS. SHARKO: No, we don't 8 want -- 9 THE WITNESS: Okay. 10 DR. THOMPSON: Yeah, 11 let's -- let's go -- this is 12 actually a natural break so... 13 THE WITNESS: Okay. 14 MS. SHARKO: Okay. 15 THE VIDEOGRAPHER: Stand by, 16 please. The time is 11:54 a.m. 17 Off the record. 18 - - - 19 (Lunch break.) 20 - - - 21 THE VIDEOGRAPHER: We are 22 back on the record. The time is 23 1:02 p.m. 24 BY DR. THOMPSON:</p>	<p>1 transformation of ovarian cancer cells or 2 that talc causes inflammation that's 3 relevant to ovarian cancer pathogenesis. 4 Q. So just to shorten that a 5 little bit, there's no credible evidence 6 that there's a plausible biological 7 mechanism for any association between -- 8 A. Yes. 9 Q. Let me finish, sir. 10 A. Sorry. 11 Q. -- between -- just so the 12 record is clear -- 13 A. Sorry. 14 Q. -- between talcum powder use 15 and ovarian cancer? 16 A. Yes. That's my testimony. 17 Q. So this morning we discussed 18 risk factors, cause, association. This 19 afternoon I'd like to delve into that 20 molecular cellular mechanism a little bit 21 more if that's okay. 22 On Page 12 of your report, 23 next to the last paragraph, you state, 24 "Taken together these findings clearly</p>
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<p>1 Q. Dr. Neel, this morning you 2 testified that you are not an 3 epidemiologist. 4 Is it fair to say that your 5 opinions in this case are focused on 6 whether or not there's credible evidence 7 that talcum powder can cause ovarian 8 cancer from a molecular standpoint? 9 A. I would say from a molecular 10 and -- and cellular standpoint. 11 Q. From a molecular and 12 cellular standpoint? 13 A. Yes. 14 Q. And it's your opinion that 15 there's no cause and effect. But is it 16 also your opinion that there's no 17 plausible biological mechanism for any 18 association between talcum powder use and 19 ovarian cancer? 20 A. I don't think there's any 21 evidence one way or the -- any credible 22 evidence one way or the other. 23 So there's no -- there's no 24 credible evidence that talc causes</p>	<p>1 show that different types of ovarian 2 cancer originate in different cell types 3 that suffer different types of mutations 4 which are unlikely to be caused by the 5 same environmental agent." 6 Explain that sentence to me. 7 A. Okay. So there is Type 1 8 tumors and there's Type 2 tumors, and the 9 Type 1 tumors are caused largely by point 10 mutations, and the Type 2 tumors are 11 caused largely by copy number 12 abnormalities or copy number variation 13 and rearrangements. And the underlying 14 mutagenic mechanisms that cause point 15 mutations and the repair defects that 16 cause point mutations are distinct from 17 the types of mutations -- mutational 18 processes that cause copy number 19 variation and translocations. 20 So an agent that does one 21 kind of genetic event is not likely to 22 cause the other. 23 Q. Do you have -- what is the 24 basis for that opinion? In other words,</p>

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<p>1 what article could you direct me to that 2 would make that same claim? 3 A. I can't cite an article 4 off -- that's general scientific 5 knowledge in my field. I can't cite a 6 specific article. 7 Q. So it's not possible in your 8 opinion that the same environmental agent 9 could cause the molecular changes in both 10 types of cancers or more than one type of 11 cancer? 12 A. It's -- I think I said it's 13 unlikely. 14 Q. Oh, unlikely. So -- 15 A. That's the word I'd like to 16 stick with, unlikely. 17 Q. -- stick with unlikely. 18 Okay. 19 A. I didn't say possible. I 20 said unlikely. 21 Q. Okay. And I wasn't trying, 22 in that case, to -- to trick you. I 23 was -- I was just trying to understand -- 24 A. Did you want to just tell me</p>	<p>1 and in some cases whole genome 2 sequencing, has so many different types 3 of mutations that you can actually 4 categorize the mutations according to 5 their carcinogenic agent. 6 So benzopyrenes have a 7 particular mutational signature. And so 8 you can actually see which forms of lung 9 cancer are caused by that signature and 10 which forms aren't. 11 So for example, nonsmokers 12 can get lung cancer, but smokers are 13 about 20 to 25 times more likely to get 14 cancer, and the cancers that come from 15 smoking have a characteristic molecular 16 signature, whereas the cancers that come 17 from -- that come in nonsmokers do not 18 have the character -- do not have the 19 same signature. So you can tell them 20 apart easily. 21 Q. And even different types of 22 cancer that are caused by smoking have 23 the -- that same molecular signature? 24 A. No, not all signature -- not</p>
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<p>1 when you're trying to trick me? 2 Q. Do you want me to give you a 3 warning before it's a trick question? 4 A. Yeah. Maybe. 5 Q. So how would you answer the 6 question does smoking cause lung cancer? 7 A. Yes. 8 Q. Even though there's some 9 types of lung cancer that it may cause 10 and there's others that it might, and it 11 might cause more than one? 12 A. There's -- 13 Q. Is that an analogy? 14 A. No, it's not an analogy. 15 Actually it makes my point quite well. 16 Because smoking causes 17 specific types of DNA changes. So the 18 carcinogenic agent in cigarette smoke 19 that causes lung cancer are benzopyrenes. 20 And there's actually a specific molecular 21 signature -- this is one of the major 22 advances that has happened in the last 23 three years primarily -- large scale 24 sequencing studies of exome sequencing,</p>	<p>1 all smoking-associated cancers have the 2 mutational signature of smoking. Only 3 the aerodigestive malignancies. 4 Q. So there are some type of 5 lung cancer that may be caused by smoking 6 that don't -- aren't caused by that same 7 mutation? 8 A. No, no, I didn't say that. 9 All -- 10 Q. Okay. I'm just trying to 11 understand. 12 A. All smoking-associated lung 13 cancers have the benzopyrene signature. 14 I don't remember the number. They have 15 different -- different -- there is 16 several major groups that have been doing 17 this work, and they have different 18 numbers of the signatures. 19 So actually one of the 20 references that I cite has one of the 21 numbering systems. So I can't tell you 22 the number. 23 But there's -- if you looked 24 at -- actually if you go to Cosmic, which</p>

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<p>1 is the website in my report, it has a 2 whole section on mutational signatures 3 and it tells you which ones are smoking 4 associated. 5 Q. And -- 6 A. And -- and the -- so the 7 small cell lung cancer, squamous cell 8 lung cancer and many but not all 9 adenocarcinomas of the lung are caused by 10 smoking largely. 11 There are some lung cancers 12 that are probably caused by radon and 13 others that are -- we don't know the 14 pathogenesis yet. 15 Q. What about when smoking is a 16 cocarcinogen? 17 A. Yeah, so it's less -- 18 less -- what do you mean by cocarcinogen? 19 Q. For example, you agree that 20 smoking and asbestos together cause -- 21 are more likely to cause cancer than 22 either by themselves? 23 A. So smoking plus asbestos are 24 dramatically cocarcinogenic for lung</p>	<p>1 reliable? 2 A. No. It's reliable insofar 3 as it's epidemiological evidence one way 4 or another for a particular disease. 5 But I should add there's 6 been extensive sequencing of ovarian 7 cancers over -- I don't remember if it 8 was 400 -- I'm blocking on whether it's 9 450 or 600 cases are in the literature. 10 It's easy to find. So it's not like 11 ovarian cancer has been sequenced. 12 That's how we know that the Type 1 tumors 13 and Type 2 tumors have completely 14 different mutational profiles. 15 Q. Okay. Well, the second 16 sentence in that paragraph is, "Studies 17 including epidemiological reports that 18 treat ovarian cancer as a single entity 19 should, in my opinion, be viewed with 20 skepticism." 21 And I guess my question 22 would -- because we have the sequencing 23 that -- sequencing that you're referring 24 to, should epidemiological studies that</p>
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<p>1 cancer. And I don't know if there's been 2 a detailed study of smoking plus asbestos 3 lung cancer that's been sequenced. 4 But I would strongly suspect 5 that mutational signature of benzopyrenes 6 is there. But I don't know that. I 7 don't know if it's been done. 8 Q. So do we need to discount 9 any literature in which sequencing has 10 not been done yet for any type of cancer? 11 A. Discount it from the 12 standpoint of what? 13 Q. Is it not reliable? 14 A. It depends what the question 15 is. I mean, what aspect of the cancer 16 are you asking about? 17 Q. I'm just asking that, if 18 literature, epidemiological literature 19 particularly, doesn't include the 20 molecular knowledge gained by sequencing 21 and other methods, should it be 22 discounted? 23 A. Discounted in terms of what? 24 Q. Should it not be considered</p>	<p>1 are treating ovarian cancer as a single 2 entity be discounted? 3 A. I didn't say that. 4 I said they should -- 5 Q. Well, I'm kind of -- I'm 6 sorry. I'm trying to -- 7 A. I stand by the wording in my 8 report. 9 Q. Well -- 10 A. They should be viewed with 11 skepticism -- 12 Q. Well, I'm trying to -- 13 A. -- because they're not the 14 same disease. 15 Q. I'm trying to determine what 16 you mean by "viewed as skepticism." Are 17 they less reliable -- 18 A. They are less scientifically 19 plausible. 20 Q. They're less scientifically 21 plausible? 22 A. It is less plausible. It is 23 implausible that a single agent acting 24 via a single carcinogenic mechanism would</p>

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<p>1 cause dramatically different mutational 2 processes leading to dramatically 3 distinct mutational signatures. 4 Type 1 tumors and Type 2 5 tumors originate in different cell types. 6 That's pretty clear. And they have 7 dramatically different mutational 8 signatures. 9 The fact that they have 10 different mutational signatures means 11 that they're caused by different 12 molecular processes. 13 Therefore, it is highly 14 unlikely that a single agent acting via a 15 single pathogenic mechanism would lead to 16 distinct molecular signatures acting in 17 different cells of origin. 18 Q. Are there risk factors and 19 protective risk factors for epithelial 20 ovarian cancer that cross all types in 21 your opinion? 22 A. I don't really -- I can't -- 23 you know, not coming to mind right away, 24 not that I know of, no.</p>	<p>1 2 tumors. 2 Q. What about age? 3 A. Well, age is -- age is just 4 due to the accumulation of mutations. 5 All mutations are more common with age. 6 So age is -- age is a contributor to all 7 forms of cancer, but that's because the 8 chances of accumulating the necessary 9 mutations by any mutational process 10 increase with age. 11 Q. What about BRCA1 and 2? 12 A. BRCA1 and 2 are primarily 13 Type -- Type 2 tumors. 14 Q. And only serous? 15 A. Well, some people would 16 call, you know, the peritoneal carcinomas 17 and the carcinosarcomas separate. But I 18 think molecularly they -- most people 19 would view them as Type 2 tumors, 20 effectively the same as serous cancer, 21 yes. 22 Q. And you're including -- 23 A. High grade serous, not the 24 low grades.</p>
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<p>1 Q. So -- 2 A. Well, so -- for example, let 3 me just -- what do you mean by all types? 4 So for example, the -- you know, obesity 5 is associated with, you know, 6 endometrioid and clear cell. But those 7 are the same type of pathogenic 8 mechanisms. 9 Q. How about the reproductive 10 risk for protective factors, for example, 11 parity, oral contraceptive use, that 12 appear to apply to all subtypes, 13 histologic subtypes, as well as Type 1 14 and Type 2. Would you agree? 15 A. Yeah, I think parity 16 probably does. But I -- that's not clear 17 that could be a single entity either. 18 That could be more than one entity. In 19 one case, it could be incessant 20 ovulation. In the other case, it could 21 be the weak -- it could be that both 22 mechanisms have been purported to explain 23 the parity effect could operate 24 differently in different Type 1 and Type</p>	<p>1 Q. And you're including 2 endometrioid and clear cell with the Type 3 1 tumors? 4 A. No. Oh, with the Type 1, 5 yeah. Sorry. Yeah, I'm a little -- it's 6 a little -- it's the postprandial thing. 7 I shouldn't have eaten anything. 8 Q. Let's go to your report on 9 Page 14. And you begin Section 3, talc 10 and ovarian cancer. And it looks like to 11 me this is where you put your major 12 opinions in bold. And it says "Opinion." 13 In the paragraph that 14 states, "Talc is chemically inert and 15 nongenotoxic," you have three references 16 there. 17 This morning you testified 18 that you only saw the Health Canada risk 19 assessment yesterday and that you had not 20 read it, correct? 21 A. I think that I -- I didn't 22 see the Health Canada actual text. I 23 must have seen something that said it was 24 possibly carcinogenic, but I don't know</p>

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<p>1 where I saw that. It might be -- I'm 2 citing the paper. I think it's the 3 Taher, et al., paper. That's what I 4 assume it is. 5 Q. Well, that's what I'm trying 6 to establish. So that when you said 7 Health Canada reviewed the literature, 8 you haven't actually read the Health 9 Canada assessment, right? 10 A. I read the -- was it Taher? 11 What are you calling it? 12 Q. Taher. 13 A. Taher. I read the Taher, et 14 al., paper -- 15 Q. Okay. 16 A. -- that said that it was 17 funded by Health Canada. 18 Q. So that's -- that's wrong 19 that Health Canada reviewed the 20 literature, correct? 21 A. It says, "The Taher, et al., 22 manuscript that was funded by Health 23 Canada." 24 So that's what I'm referring</p>	<p>1 could have been a little bit -- 2 Q. Yeah. 3 A. -- sloppy writing. 4 Q. And it says, "It focuses 5 primarily on a meta-analysis by Taher." 6 So it -- but you're saying that you meant 7 Taher reviewed the literature, not Health 8 Canada? 9 A. Yes. 10 Q. Okay. Let's go ahead and 11 mark the three documents that you 12 referred to in that paragraph now that we 13 have it clear that it wasn't the Health 14 Canada, it was the Taher article. 15 (Document marked for 16 identification as Exhibit 17 Neel-18.) 18 BY DR. THOMPSON: 19 Q. The first is the letter that 20 you referred to as -- from the FDA to 21 Samuel Epstein will be Exhibit 18. 22 DR. THOMPSON: The IARC 23 Volume 93 published in 2010. 24 MS. SHARKO: No, no, no,</p>
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<p>1 to. 2 Q. Okay. So is it your 3 understanding that Health Canada 4 commissioned Taher and his group to do a 5 meta-analysis, and that's what Health 6 Canada relied on in part on their risk 7 assessment, correct? 8 A. That's my understanding, 9 yes. 10 Q. But each time that you're 11 referring to Health Canada in your 12 report, you're actually referring to the 13 Taher paper? 14 A. That's correct. 15 Q. Because you have not read -- 16 actually read the Health Canada risk 17 assessment? 18 A. That's correct. I read the 19 Taher, et al., manuscript, funded by 20 Health Canada, as it says in my report. 21 Q. Okay. Well, your report 22 actually says Health Canada had reviewed 23 the literature. 24 A. So I -- maybe it was --</p>	<p>1 you're marking your notes. 2 DR. THOMPSON: Oh, see 3 you're looking after me. 4 MS. SHARKO: I'm watching 5 out for you. 6 (Document marked for 7 identification as Exhibit 8 Neel-19.) 9 DR. THOMPSON: 19 then will 10 be the -- will you all take all of 11 these. 12 -- will be the IARC 2010 13 monograph on non-asbestiform talc. 14 (Document marked for 15 identification as Exhibit 16 Neel-20.) 17 DR. THOMPSON: And the third 18 will be the Taher systematic 19 review and meta-analysis that was 20 commissioned by Health Canada. 21 That's all I have with that one. 22 BY DR. THOMPSON: 23 Q. So let's go to your first 24 opinion. That talc is chemically inert.</p>

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<p>1 What do you mean by 2 chemically inert? 3 A. I mean it doesn't directly 4 damage -- in the context of this 5 statement it doesn't directly damage DNA. 6 It doesn't cause DNA damage. 7 Q. Is it biologically inert in 8 your opinion, or are you -- are you using 9 those two terms interchangeably? 10 A. No, I'm saying the -- no, 11 I'm not using those terms 12 interchangeably. 13 Q. Okay. 14 A. In the -- in the context 15 of -- you know, in the body it can cause 16 granulomatous inflammation or granulomas. 17 But that's not the kind of inflammation 18 that's associated with carcinogenesis. 19 But it doesn't -- it's -- 20 it's chemically inert in the sense that 21 if you have it on the table, it's not 22 highly reactive with, you know, typical 23 substances. So -- 24 Q. So --</p>	<p>1 inflammatory reaction of some type in 2 human -- 3 A. It causes -- sorry. 4 Q. -- and animal tissues? 5 A. It causes granulomatous 6 reactions. Some people would call that 7 an inflammatory reaction. Some people 8 would call it a foreign body reaction. 9 Some people just call it a granuloma. 10 But it's not the kind of 11 inflammation that Balkwill or Hanahan 12 were referring to in terms of 13 carcinogenesis. 14 Q. And it certainly causes an 15 acute inflammatory reaction as well? 16 A. It causes granulomatous 17 inflammation. 18 Q. When it's used for 19 pleurodesis, what type of reaction is it? 20 A. It's a granulomatous and 21 fibrotic response. 22 Q. Okay. So granulomatous and 23 fibrotic response. 24 And what's your basis for</p>
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<p>1 A. And if you put it on cells 2 it doesn't damage DNA. 3 Q. Okay. So to you chemically 4 inert here is being used as not directly 5 damaging DNA? 6 A. Not directly or indirectly 7 damaging DNA. And that's in the context 8 of this statement. But it's also 9 chemically inert in the sense that it's 10 not highly reactive with most substances. 11 So... 12 Q. Okay. So not directly or 13 indirectly damaging DNA in the cell. And 14 not reactive chemically -- 15 A. With most substances. 16 Q. With most substances, okay. 17 But you would agree that 18 it's not biologically inert? 19 A. No, not in certain 20 locations. It can cause -- it's a 21 foreign body and it can cause a foreign 22 body reaction. 23 Q. In -- so that you -- you 24 agree that talcum powder does cause an</p>	<p>1 your statement that that is not the type 2 of response that Balkwill and others are 3 talking about? 4 A. Because the type of -- I'm 5 aware of the literature about 6 inflammation and cancer. And that's 7 typically type -- you know, the sort of 8 infiltration with activated macrophages, 9 infiltrated neutrophils. That's not the 10 kind of thing you get in a chronic body 11 reaction. 12 And there's -- and even more 13 to the point, there's no association of 14 granulomas with ovarian cancer that has 15 been published to my knowledge. 16 Q. But can you direct me to a 17 particular article? 18 A. I'd have to, you know, go 19 back and look at my literature to give 20 you a -- I can't give you that offhand. 21 But it's general knowledge 22 that granulomas are not associated with 23 ovarian cancer pathogenesis. 24 Q. But you do agree that</p>

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<p>1 granulomas and granulomas caused by talc 2 are well reported in ovarian pathology? 3 A. No, I would not agree with 4 that at all. Absolutely not. 5 Q. You are telling me that talc 6 granulomas are not reported in ovarian 7 tissue? 8 A. Not to my knowledge. And, 9 in fact, the case -- the literature that 10 I cited in my report, I'd have to pull 11 out the exact references, reported talc 12 particles in the ovary with no associated 13 granulomatous inflammation. 14 Q. Have you looked at a GYN 15 pathology textbook lately? 16 A. I would have no occasion to 17 look at a GYN pathology textbook. 18 Q. Would it surprise you if 19 virtually every GYN pathology textbook 20 would have a section on foreign body 21 granulomas including talc? 22 A. I would have to look at 23 exactly what you're talking about. 24 Q. I didn't bring a textbook</p>	<p>1 form. Misstates the testimony. 2 THE WITNESS: Can you repeat 3 the question? 4 BY DR. THOMPSON: 5 Q. Well, let me just ask it. 6 Is -- is fibrous talc chemically inert? 7 A. I -- I have no specific 8 opinion on fibrous talc. My opinions 9 are -- are related to the talc that was 10 used in the papers that I reviewed and 11 the epidemiological studies that I 12 reviewed. And whatever is in those 13 products my opinion relates to. 14 Q. Okay. Is asbestos 15 chemically inert, or do you not have an 16 opinion? 17 A. I have an opinion -- it's -- 18 it's not cellularly inert. But I don't 19 have -- I don't have a great deal of 20 detailed knowledge on asbestos 21 pathogenesis. That's not the topic of my 22 research and that's not the topic of my 23 analysis for the purposes of this report. 24 Q. So for this case you are not</p>
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<p>1 but I do have an example. 2 Do those opinions that, in 3 your words, talc is chemically inert, 4 apply to Johnson's Baby Powder in your 5 opinion? 6 A. Yes. 7 Q. And apply to Shower to 8 Shower I assume? 9 A. Yes. 10 Q. Would that opinion apply to 11 fibrous talc? 12 A. As I said earlier today, 13 I'm -- I'm referring to any of the talc 14 that was used in the studies that I 15 evaluated for the purposes of writing my 16 report. So it does not say one way or 17 the other fibrous talc. It has to do 18 with the specific experiments that are 19 cited in my report that have to do with 20 talc and ovarian cancer pathogenesis. 21 Q. So it's fair to say that you 22 don't have an opinion as to whether 23 fibrous talc is chemically inert? 24 MS. SHARKO: Object to the</p>	<p>1 going to be giving opinions as to the 2 cellular effects of asbestos; is that 3 fair to say? 4 A. That's correct. 5 (Document marked for 6 identification as Exhibit 7 Neel-21.) 8 BY DR. THOMPSON: 9 Q. Exhibit 21 is an article 10 titled "Foreign Body Granulomas in Normal 11 Ovaries." I don't want to spend a whole 12 lot of time with this. 13 You can look over at -- it 14 describes a study at Hopkins, published 15 in Obstetrics and Gynecology, that ACOG 16 Green Journal, that looked at 100 17 consecutive cases of oophorectomy for 18 benign disease. And they found that, I 19 believe it was 9 percent of normal 20 ovaries had cortical granulomas 21 containing a foreign body-type giant cell 22 and associated with a foreign body which 23 consisted of magnesium silicate that they 24 postulated was talc or asbestos.</p>

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<p>1 Does that sound like a fair 2 summary of this paper? 3 A. Well, I don't know. I'd 4 have to sit here and read it to really be 5 clear. 6 I mean, you know, I'm not 7 going to be able to accept your 8 conclusions without reading the whole 9 paper. 10 Do you want me to read the 11 paper? 12 Q. Probably not. Let's see if 13 we can just find a summary statement 14 that's not mine, that's the authors. 15 A. Well, I'm not going to agree 16 until I read the whole paper. Because 17 the summary statement would be their 18 opinions of the data, not mine. 19 Q. Okay. Do you agree that 20 this paper reports foreign body 21 granulomas in normal ovaries from Johns 22 Hopkins? 23 A. That's the title of, but I 24 mean, just -- that's the title of the</p>	<p>1 BY DR. THOMPSON: 2 Q. Well Group 3 had granulomas. 3 Group 4 had a foreign body. 4 A. There's nothing in there 5 that says that that's caused by talc. 6 MS. SHARKO: If we're going 7 to use the paper, why don't you -- 8 BY DR. THOMPSON: 9 Q. Okay. Go ahead and take -- 10 go ahead and take a minute to review it. 11 A. All right. There's -- I 12 mean there's no evidence that this is -- 13 there's nothing that says that it's 14 caused by talc. 15 MS. SHARKO: Wait. First, 16 read the paper. Then she'll ask 17 you a question. Okay. There's no 18 question pending. I don't think. 19 DR. THOMPSON: I don't think 20 so either. But I'm not sure. 21 MS. SHARKO: Okay. Well if 22 there is, you'll ask it again. 23 BY DR. THOMPSON: 24 Q. So did this article report</p>
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<p>1 paper. But again I just want to -- just 2 in casually pursuing it, cases, on the 3 first page, it says, "Cases in which 4 there were foci of reticular stroma with 5 or without inflammation" -- oh, sorry. 6 Q. Yeah. 7 A. "Cases in which there were 8 foci of reticular stroma with or without 9 inflammation that have been classically 10 referred to as 'cortical granulomas' but 11 have been referred to as endometriosis by 12 others." 13 And in cases, and then these 14 giant cell ones which may be cortical -- 15 which may be, you know, granulomas. 16 But there's -- it seems -- 17 Q. Well, Group -- Group 3 -- 18 MS. SHARKO: Let him finish. 19 He said, "but there." 20 THE WITNESS: Group 3 says 21 has been described -- I'm not a 22 gynecological pathologist. I 23 can't comment on whether that's 24 really endometriosis or not.</p>	<p>1 on foreign body granulomas that, when 2 tested using computer-assisted x-ray 3 analysis of the crystalline foreign body, 4 they were determined to be composed 5 largely of magnesium and silicone. 6 A. Yes. Okay. Well, that's 7 what the paper says. I am not an expert 8 in how one decides what a particle is. 9 So I can't comment whether this is 10 consistent with talc or not. 11 Q. Okay. 12 A. But I will -- can I finish? 13 I will notice that 14 44 percent of these patients had a 15 previous laparotomy -- a previous 16 laparotomy so that raised -- they could 17 have gotten from talc from the talcum 18 powder in the surgical gloves which was 19 probably present at the time. 20 So this is -- you know, I 21 don't think it's questionable that talc 22 can cause granulomas. The question is 23 whether perineal talc causes granulomas. 24 And there's absolutely no evidence in</p>

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<p>1 this paper that I can see from my reading 2 that perineal talc causes granulomas in 3 the ovary. 4 Q. But talc can cause granuloma 5 in the ovary, correct? 6 A. I think that's -- yeah, talc 7 can definitely cause granulomas probably 8 in many body cavities, but I just to -- 9 can I also -- can I finish, please? 10 Q. There's no question on the 11 table. 12 A. You just asked a question. 13 Q. Well, you answered it. 14 A. No. 15 MS. SHARKO: You can -- no. 16 Finish your answer. 17 THE WITNESS: The finishing 18 of my answer is that I think the 19 relevant point is foreign body 20 granulomas in normal ovaries, 21 there's absolutely no evidence in 22 these ovaries of pre neoplastic 23 changes. So I think this actually 24 strongly supports my argument. It</p>	<p>1 cobalt? 2 A. As again, my opinions are 3 based on and restricted to the talc that 4 was used in the papers that I reviewed 5 and epidemiological studies that I 6 commented on in my report. So I can't 7 comment on any of these other questions 8 involving heavy metals or stuff like 9 that. 10 Q. I understand. But I'm going 11 to ask them regardless. 12 A. That's fine. 13 Q. So be patient. 14 A. I'm patient. 15 Q. So it's really irrelevant to 16 you whether or not talcum powder products 17 like Johnson's Baby Powder contain heavy 18 metals? 19 A. It's irrelevant to me in the 20 context of whether they cause ovarian 21 cancer, because I'm basing my opinion on 22 the biological experiments using said 23 products and the epidemiological studies 24 that included or were focused on mainly</p>
Page 235	Page 237
<p>1 doesn't argue against it. 2 BY DR. THOMPSON: 3 Q. Are there pre-neoplastic 4 changes that can be observed in ovaries? 5 A. In ovaries, yes. 6 Q. What are those? 7 A. So some cortical inclusion 8 cysts can show evidence of metaplastic 9 change. But I -- they didn't just remove 10 the ovaries. I assume they removed the 11 fallopian tubes too. You don't need to 12 just remove ovaries. 13 Q. You have no idea whether 14 they did or not, do you? 15 A. Well, give me some time 16 here. I don't know, but as a -- you 17 know, as a gynecological oncologist, you 18 would know that. 19 Q. And you're not a GYN 20 pathologist as you just stated? 21 A. That's correct. 22 Q. Does the opinion about talc 23 being chemically inert, would that apply 24 to heavy metals like chromium, nickel, or</p>	<p>1 the use of said products. 2 Q. And it's irrelevant as far 3 as a biologically plausible mechanism as 4 well. Would you agree with that 5 statement? 6 A. My evidence -- my statement 7 on biological plausibility is based on 8 the purported evidence supporting the 9 case that talc is involved in ovarian 10 cancer, based on biological experiments, 11 or the absence of proof in those 12 experiments that talc causes any evidence 13 of ovarian cancer. 14 So it's based on that. 15 Q. And are chemicals that are 16 known to be contained in Johnson's Baby 17 Powder as fragrances, would your opinion 18 that they're chemically inert also be 19 irrelevant? 20 A. I'm not aware of what 21 chemicals are or are not in Johnson's 22 Baby Powder, so I can't comment on that 23 one way or the other. 24 Q. So you don't have an opinion</p>

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<p>1 as to whether styrene, cumarin, eugenol, 2 d-limonene, p-Cresol, musk ketone, and 3 benzophenone, which are all possible or 4 known carcinogen, would render talcum 5 powder not chemically inert? 6 MS. SHARKO: Object to the 7 form of the question. 8 BY DR. THOMPSON: 9 Q. Did you understand the 10 question? 11 A. That was sort of a double 12 negative. 13 Q. It was. 14 A. I'm trying to parse it. 15 And, you know -- 16 Q. Fair enough. 17 A. -- my blood sugar dropped 18 after lunch. 19 Q. Right. 20 A. It's hard enough. 21 Q. Are chemicals such as -- 22 that are known to be possible or 23 suspected carcinogens -- are chemicals 24 like styrene, cumarin, eugenol,</p>	<p>1 products are chemically inert? 2 A. No, I -- 3 MS. SHARKO: Objection. 4 Asked and answered. 5 THE WITNESS: As I explained 6 this morning it's impossible for 7 me to do any experiments under the 8 conditions of my contractual 9 obligation to be an expert witness 10 in this case. 11 So, no, I did not perform 12 any experiments, nor do I plan to. 13 BY DR. THOMPSON: 14 Q. Can you refer me to studies 15 that explicitly state that Johnson's Baby 16 Powder and Shower to Shower products are 17 chemically inert? 18 A. No, I cannot refer you to 19 studies that state that. 20 Q. Regarding your opinion, talc 21 does not cause mutations, you describe in 22 your report that cancer is a disease that 23 involves mutations and specific genes, 24 right?</p>
Page 239	Page 241
<p>1 d-limonene, p-Cresol, musk ketone, and 2 benzophenone chemically inert? 3 MS. SHARKO: I object to the 4 form of the question. It lacks 5 foundation and it assumes facts 6 not in evidence. 7 THE WITNESS: I am not a 8 toxicologist. So I can't comment 9 on any of those specific 10 chemicals. 11 BY DR. THOMPSON: 12 Q. So -- 13 A. And I don't have any 14 knowledge as to whether or not they're in 15 Johnson & Johnson products. So I can't 16 comment. 17 Q. So you would not be giving 18 any opinions as to whether those 19 chemicals that I just named off were 20 chemically inert or not? 21 A. No, I will not be giving an 22 opinion on that. 23 Q. Did you perform any studies, 24 experiments to test whether talcum powder</p>	<p>1 A. Yes. 2 Q. And -- 3 A. Where are we in my report, 4 please, so I can follow along. 5 Q. We're still on Page 14 with 6 those opinions -- 7 A. Oh, okay. All right. 8 Q. -- opinions in bold? 9 A. I see. Sorry, yeah. 10 Q. Do you agree that 11 carcinogens can be genotoxic or 12 non-genotoxic? 13 A. Promoters can be -- again, 14 it comes down to a little bit of a 15 semantic argument. I mean, primary 16 carcinogens are mutagens. Some people 17 would -- as I said earlier this morning, 18 some people would class tumor promoters 19 that are not direct mutagens, as 20 carcinogens. 21 So I prefer to discriminate 22 between initiating events and promotion 23 events. 24 Q. With a definition of</p>

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<p>1 carcinogenesis that includes initiation 2 and promotion, can you agree that 3 carcinogen can either be genotoxic or 4 non-genotoxic? 5 A. Yes. 6 Q. But your opinion is for 7 initiation purposes, that carcinogens 8 have to be genotoxic; is that correct? 9 A. Yes. 10 Q. And you are 100 percent 11 confident in that opinion? 12 A. They have to be directly or 13 indirectly genotoxic. They have to cause 14 damage to DNA, otherwise they are not 15 carcinogens. 16 Q. And what do you -- what do 17 you mean by indirectly genotoxic? 18 A. If they indirectly cause 19 reactive oxygen generation and the 20 reactive oxygen species cause the -- 21 cause the mutations, that would be 22 indirectly genotoxic. 23 Q. Wouldn't -- wouldn't some 24 scientists refer to that indirect</p>	<p>1 epidemiological studies can address that 2 question directly. 3 Q. That -- that was -- yeah. 4 That answered my question. Thanks. 5 A. I -- well, not standard 6 epidemiological studies. New types of 7 epidemiological approaches could in 8 principle do that. But that would be a 9 new approach. 10 Q. So you're really referring 11 to the cellular studies when you give the 12 opinion that talc does not cause 13 mutation, correct? 14 A. Yes. And the fact that it 15 was tested in the Ames test for example, 16 and other standard toxicity tests. 17 Q. I'll get to that in a 18 minute. 19 Does that opinion apply to 20 asbestos? 21 A. I have no opinion 22 specifically on asbestos, as I told you 23 earlier. 24 Q. And same thing with talc</p>
Page 243	Page 245
<p>1 mechanism as non-genotoxic? 2 A. I -- I can't comment on what 3 other scientists would refer to. If you 4 want to give me a specific literature 5 reference I can help out on that. 6 Q. Okay. I may need some help 7 with that one. Because I believe that 8 I've seen that in the literature. 9 And does the opinion that 10 talc does not cause mutations apply to 11 Johnson's Baby Powder? 12 A. It applies -- my opinions 13 again -- I'm sorry to be repetitive -- 14 but my opinions refer to any of the 15 studies, epidemiological or biological, 16 that included Johnson & Johnson baby -- 17 baby product and baby -- baby shower, and 18 to talc used in said studies that was not 19 from Johnson & Johnson. 20 Q. You would agree that your 21 opinion that talc does not cause 22 mutations is not based on epidemiological 23 literature, right? 24 A. I don't believe that</p>	<p>1 fiber or fibrous talc? 2 A. Again, as I said earlier, my 3 comments are not relevant to that -- or 4 not -- 5 Q. How about heavy -- 6 A. My comments are not germane 7 to -- I have no comments on that. Sorry. 8 Q. And -- no apologies needed. 9 And how about the chemical 10 carcinogens that are possibly in Baby 11 Powder? 12 A. I -- 13 MS. SHARKO: Object. Object 14 to the form of the question. 15 Lacks foundation. 16 THE WITNESS: So, same -- 17 same answer as I said before. 18 My -- my opinions are restricted 19 to Johnson & Johnson products, 20 effects on cellular or animal 21 models in the context of mutation 22 generation. 23 BY DR. THOMPSON: 24 Q. And did you perform any</p>

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<p style="text-align: right;">Page 246</p> <p>1 studies testing whether talcum powder 2 products cause mutations? 3 MS. SHARKO: You know, asked 4 and answered. This is about the 5 seventh time you've answered that. 6 DR. THOMPSON: The question 7 has not been -- 8 MS. SHARKO: He has not done 9 any studies other than research. 10 DR. THOMPSON: I'm -- but 11 I'm allowed to ask about a test 12 for mutations. It's not the same 13 question. 14 BY DR. THOMPSON: 15 Q. Go ahead. 16 A. I have performed no studies 17 on Johnson & Johnson Baby Powder, baby 18 showers, any Johnson & Johnson product or 19 any form of talc in my own laboratory, 20 because I am prohibited from so doing as 21 a consequence of my institution's 22 conflict of interest rules. 23 Q. Can you refer me to any 24 study that explicitly states that</p>	<p style="text-align: right;">Page 248</p> <p>1 particles and fibers? 2 MS. SHARKO: Wait. I 3 couldn't -- somebody coughed and I 4 couldn't hear the question. Can 5 you say it again? 6 BY DR. THOMPSON: 7 Q. Do you agree that standard 8 genotoxicity tests are not reliable for 9 the determination of the genotoxicity of 10 particles and fibers? 11 A. I'm not an expert on 12 toxicology. So I don't have a lot of 13 experience with genotoxicity of particles 14 and fibers. 15 But my point was that it's 16 not genotoxic, and that I stand by. 17 Q. So you're saying it's not 18 genotoxic, but you don't have any 19 experience with genotoxicity of particles 20 and fibers? 21 A. No, I'm saying that the 22 standard genotoxicity assays were done on 23 talc and it's not genotoxic. Scientists 24 reach conclusions based on assays and</p>
<p style="text-align: right;">Page 247</p> <p>1 Johnson's Baby Powder and Shower to 2 Shower don't -- do not cause mutations? 3 A. Not offhand, no. 4 Q. Your next opinion is that 5 talc is not genotoxic. And you state as 6 support of that, that -- on Page 16, that 7 "talc is universally acknowledged to be 8 non-genotoxic in standard mutagenesis 9 assays." 10 What assays are you 11 referring to? 12 A. These are the genes test 13 which is a test of mutations. I forgot 14 the name of the test, but it's a test of 15 chromosomal segregation defects. 16 Q. And you -- 17 A. Actually, I just want to 18 state that, again, all of the regulatory 19 agencies agree with that statement, 20 including the FDA, and -- well, certainly 21 IARC. 22 Q. Do you agree that standard 23 genotoxicity tests are not reliable for 24 the determination of the genotoxicity of</p>	<p style="text-align: right;">Page 249</p> <p>1 experiments, not based on suppositions or 2 hypotheses. 3 Q. My question was, are you 4 aware that the genotoxicity testing is 5 not accurate with particles and fibers? 6 MS. SHARKO: So I object to 7 the form of the question. That's 8 not what you asked him. If that's 9 your question, he'll be happy to 10 answer that. 11 DR. THOMPSON: Okay. I'll 12 ask that question then. 13 BY DR. THOMPSON: 14 Q. Are genotoxicity tests 15 accurate when testing particles and 16 fibers? 17 A. Accurate in terms of what? 18 Q. Reliable. 19 A. Reliable in terms of what? 20 Q. Well, your statement is 21 "talc is universally acknowledged to be 22 non-genotoxic in standard mutagenesis 23 assays." 24 And I'm asking you, do you</p>

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<p>1 have knowledge regarding the reliability 2 of those tests in products that are -- 3 have particles or fibers? 4 A. The tests are extremely 5 reliable. They measure genotoxicity. 6 Whether you use a particle, fiber, any 7 chemical, they measure genotoxicity. 8 Q. Okay. 9 A. That's not -- the issue is 10 whether there are other types of assays 11 that might yield a different result, and 12 I have no expertise on particles and 13 fibers beyond the fact that standard 14 assays of genotoxicity do not show any 15 mutagenesis. 16 And that's -- that's true to 17 the best of my knowledge. 18 (Document marked for 19 identification as Exhibit 20 Neel-22.) 21 BY DR. THOMPSON: 22 Q. This is -- I just marked 23 Exhibit 22. It is an article titled 24 "Mechanisms of Genotoxicity of Particles</p>	<p>1 be reasonable. 2 MS. SHARKO: No, I -- I 3 disagree. I don't know that 4 that's what we've always done. If 5 you want to use your deposition 6 time to have him read it, then 7 we're not going off the record. 8 DR. THOMPSON: I'm going to 9 use my deposition time to have him 10 look at the chart on Page 70. 11 THE WITNESS: I can see the 12 chart. 13 BY DR. THOMPSON: 14 Q. Is that chart consistent 15 with what your opinions would be 16 regarding genotoxicity of particles and 17 fibers? 18 A. As I said, I'm not an expert 19 in particle and fibers. And I have no 20 comment on this paper because I would 21 have to really read the entire thing. 22 And also I would have to go through the 23 literature and see what's been written 24 since 2012 -- 2002 on this subject.</p>
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<p>1 and Fibers." 2 Have you seen this article 3 before? 4 A. No. 5 Q. Do you -- would you like to 6 take a minute to look through it? 7 A. I mean it will take me at -- 8 at least an hour to read this paper. 9 Q. Okay. Well, we won't spend 10 an hour. Let's just go to the chart -- 11 MS. SHARKO: Well, no, it's 12 not fair to ask him about it if 13 he's not seen it before or read 14 it. 15 DR. THOMPSON: Okay. We'll 16 go off the record for an hour 17 then. It will be fine. 18 MS. SHARKO: No, why should 19 we go off the record? You want to 20 use this -- 21 DR. THOMPSON: Because 22 that's what we've always done when 23 an expert needs longer time to go 24 through an article than seems to</p>	<p>1 Again, 2002 is a long time 2 ago in cancer biology. And I have no 3 knowledge offhand whether this is even 4 considered to be state of the art. 5 Q. Okay. All right. We'll 6 move on. 7 A. So I have no comment. 8 Q. We'll move on. Did you 9 perform any studies to test whether 10 talcum powder products are not genotoxic? 11 MS. SHARKO: Objection. 12 Asked and answered. 13 BY DR. THOMPSON: 14 Q. You can answer again. 15 A. As I said -- 16 Q. You don't have to give the 17 explanation. Just say yes or no. 18 A. No. 19 MS. SHARKO: No, you should 20 give a complete answer. You can't 21 just keep asking a question and 22 hope for a sound byte. He hasn't 23 done any studies. We stipulated 24 that.</p>

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<p>1 MS. O'DELL: Object to the 2 form, Susan. 3 DR. THOMPSON: Hey, I don't 4 need the -- I do not need the 5 speaking objection. 6 MS. O'DELL: Or coaching the 7 witness. 8 MS. SHARKO: He clearly 9 doesn't need coaching, especially 10 when you've asked the same 11 question like ten times. 12 MS. O'DELL: Not that that's 13 restrained you at all. It's 14 coaching the witness. Object to 15 form is the appropriate objection. 16 BY DR. THOMPSON: 17 Q. Can you refer me to any 18 studies that explicitly state that 19 Johnson & Johnson Baby Powder and Shower 20 to Shower are not genotoxic? 21 MS. SHARKO: Objection. 22 Asked and answered. 23 THE WITNESS: I think you 24 asked that already, but no.</p>	<p>1 humans or would that include animals as 2 well? 3 A. That would refer to both. 4 Q. You do agree, then, that 5 talcum powder is known to be inflammatory 6 in other tissues? 7 MS. SHARKO: Object to the 8 form. 9 THE WITNESS: You have asked 10 that in a different way before. 11 But let me try to give the same 12 answer so that it's clear. 13 If you inject talc into a 14 body cavity, it can cause a 15 foreign body reaction, which some 16 people cause -- call granuloma -- 17 granulomatous inflammation. 18 So yes, talc can cause 19 foreign body reactions or 20 granulomas. 21 However, to my knowledge, 22 there is no evidence that talc 23 causes other -- causes 24 cancer-associated inflammation,</p>
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<p>1 BY DR. THOMPSON: 2 Q. And your opinion is that, on 3 Page 14, talc does not cause inflammation 4 in the female genitourinary tract. What 5 are you basing that opinion on? 6 A. I just want to clarify. I 7 was referring -- I was a little -- not 8 very clear in saying I'm referring to the 9 type of inflammation that usually is 10 associated with cancer. 11 So talc will potentially 12 cause a foreign body granuloma in the 13 female genital tract. But there's no 14 evidence that foreign body granulomas are 15 associated with ovarian cancer 16 pathogenesis. 17 So I may have been a little 18 loose with my terminology with that 19 particular part. But the point is that 20 talc does not cause precancerous 21 inflammation or cancer-promoting 22 inflammation in the female genital tract. 23 That's my point. 24 Q. Is that referring to female</p>	<p>1 particularly in the female genital 2 tract where the direct experiment 3 has been done and indirect 4 experiments have been done. And 5 the evidence, including some 6 evidence that you showed me, is 7 inconsonant with the idea that 8 it's causing cancer-promoting 9 inflammation. 10 BY DR. THOMPSON: 11 Q. And you're familiar with the 12 animal studies done with talc, correct? 13 A. Which animals studies? I'm 14 familiar with several animal studies. If 15 you want to cite a particular one, I'm 16 happy to talk about it. 17 (Document marked for 18 identification as Exhibit 19 Neel-23.) 20 BY DR. THOMPSON: 21 Q. I'll mark as Exhibit 23 as 22 the Keskin rat study. Have you seen this 23 one, Dr. Neel? 24 A. Yes, I cite that in my</p>

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<p>1 report.</p> <p>2 Q. Okay. And the Keskin</p> <p>3 study -- did find that the rats that were</p> <p>4 exposed to talc had evidence of foreign</p> <p>5 body reaction and infection along with an</p> <p>6 increase in inflammatory cells in the</p> <p>7 genital tissues, right?</p> <p>8 A. So can we be -- let's --</p> <p>9 let's just go through the findings</p> <p>10 actually on page -- the first page. "In</p> <p>11 both groups exposed to talc, evidence of</p> <p>12 foreign body reaction" --</p> <p>13 MS. SHARKO: Slow down.</p> <p>14 Slow down.</p> <p>15 THE WITNESS: Sorry.</p> <p>16 -- "and infection along with</p> <p>17 an increase in inflammatory</p> <p>18 cells."</p> <p>19 So again, foreign body</p> <p>20 reaction I've already stipulated</p> <p>21 can be caused by talc. However,</p> <p>22 the infection causes the</p> <p>23 inflammation.</p> <p>24 So I mean, these rats got</p>	<p>1 the infection came from, correct?</p> <p>2 A. No. But I do know that</p> <p>3 infections cause inflammatory cells to</p> <p>4 come there. So you can't conclude</p> <p>5 anything about the nature of the</p> <p>6 inflammation. If you have an infection,</p> <p>7 you will definitely get white blood cells</p> <p>8 coming in, as any first year medical</p> <p>9 student knows.</p> <p>10 Q. Are you familiar with the</p> <p>11 Hamilton study?</p> <p>12 A. Yes.</p> <p>13 Q. Another rat study.</p> <p>14 (Document marked for</p> <p>15 identification as Exhibit</p> <p>16 Neel-24.)</p> <p>17 BY DR. THOMPSON:</p> <p>18 Q. And in this study with</p> <p>19 rats --</p> <p>20 MR. ZELLERS: Is this</p> <p>21 Exhibit 24?</p> <p>22 DR. THOMPSON: I'm sorry.</p> <p>23 Yes, Exhibit 24.</p> <p>24 BY DR. THOMPSON:</p>
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<p>1 infected. So infection will cause</p> <p>2 inflammation. But talc is not</p> <p>3 known to cause infection, as far</p> <p>4 as I know.</p> <p>5 So this study is not</p> <p>6 relevant to the issue, except for</p> <p>7 the fact that it does cause</p> <p>8 granulomas, which was seen in</p> <p>9 other studies.</p> <p>10 BY DR. THOMPSON:</p> <p>11 Q. So you think that the</p> <p>12 infection is -- that resulted in these</p> <p>13 animals were completely unrelated to the</p> <p>14 talc?</p> <p>15 A. I can't comment on what the</p> <p>16 sterile technique was in this laboratory</p> <p>17 or what other agents they were exposed to</p> <p>18 in this laboratory.</p> <p>19 But I think that it's not</p> <p>20 alleged as far as I understand that talc</p> <p>21 causes infections as part of the</p> <p>22 plaintiffs' case.</p> <p>23 Q. So you don't know one way or</p> <p>24 the other, as far as this study, where</p>	<p>1 Q. The treated animals showed</p> <p>2 focal areas of papillary change on the</p> <p>3 surface epithelium, correct?</p> <p>4 A. That's what they reported,</p> <p>5 yes.</p> <p>6 Q. The authors did not conclude</p> <p>7 that the papillary changes represented</p> <p>8 first stage in development of a surface</p> <p>9 papillary epithelial neoplasm, right?</p> <p>10 A. Excuse me? Can you repeat</p> <p>11 the question.</p> <p>12 Q. Yeah, the authors --</p> <p>13 A. And what review? Refer</p> <p>14 me --</p> <p>15 Q. Well, let's just -- let's</p> <p>16 just read the authors' conclusions.</p> <p>17 A. Sure.</p> <p>18 Q. We'll just leave it at that</p> <p>19 one. I can't find my spot.</p> <p>20 You mentioned earlier that</p> <p>21 you did not know why the FDA removed</p> <p>22 powder from exam and surgical gloves,</p> <p>23 right?</p> <p>24 A. I didn't know that the FDA</p>

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<p>1 did it, and I certainly didn't know why 2 they did it. 3 (Document marked for 4 identification as Exhibit 5 Neel-25.) 6 BY DR. THOMPSON: 7 Q. Exhibit 25 is the FDA 8 register. 9 MR. ZELLERS: Do you have 10 copies? 11 DR. THOMPSON: Oh, I do. 12 Sorry. 13 BY DR. THOMPSON: 14 Q. Beginning on the bottom 15 right of that first page, "Banned 16 devices, powdered" -- sugar -- "surgeon's 17 gloves, powdered patient examination 18 gloves and absorbable powder for 19 lubricating surgeon's glove." 20 So does that tell you that 21 the FDA banned powder use on gloves? 22 A. Sounds like it. 23 MS. SHARKO: But again, he 24 hasn't seen this. If you want to</p>	<p>1 A. Yes. December 2016. 2 Q. And in the first paragraph 3 on purpose, in the executive summary the 4 document states, "However" -- well, sorry 5 about that. 6 "Various types of powder 7 have been used to lubricate gloves so 8 that wearers could don the gloves more 9 easily." 10 MS. SHARKO: Wait, where are 11 you? 12 THE WITNESS: The bottom -- 13 DR. THOMPSON: The bottom of 14 the first paragraph under 15 executive summary, "Purpose and 16 coverage of the final rule." 17 BY DR. THOMPSON: 18 Q. "However, the use of powder 19 on medical gloves presents numerous risks 20 to patients and healthcare workers, 21 including inflammation, granulomas and 22 respiratory allergic reactions." 23 Did I read that right? 24 A. You read it right. But it's</p>
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<p>1 -- 2 DR. THOMPSON: Well, he can 3 tell me if he needs to -- he can 4 tell me if he needs to see it. 5 He doesn't even know how -- 6 what my question is going to be. 7 The first was what was the 8 title of the regulation. 9 THE WITNESS: The title is 10 "Banned devices: Powdered 11 surgeon's gloves, powdered patient 12 examination gloves, and absorbable 13 powder for lubricating a surgeon's 14 gloves." 15 BY DR. THOMPSON: 16 Q. So I -- I read it correctly 17 too, right? 18 A. I think so. 19 Q. And this was published 20 December 19th of 2016, right? 21 A. Oh, I'm sorry, you're 22 asking? December -- where does it say 23 where it's published? 24 Q. At the top of the page.</p>	<p>1 a poorly written sentence, so it's not 2 clear what refers to what. 3 Q. But it states that 4 inflammation was -- and granulomas were 5 at least part of the reason why powder 6 was removed from surgical gloves and 7 examination gloves, right? 8 A. So the way the -- the way 9 the sentence is written is not very 10 accurate. So it's not clear whether they 11 are saying inflammation of a different 12 type and the granulomas. Or whether 13 they're -- they're basically saying 14 they're both saying the same thing. 15 And it's also not saying 16 whether the risk is to the patient or to 17 the healthcare worker. And it's also not 18 saying that it involves talc. 19 So it's a very poorly 20 written sentence that doesn't allow me to 21 offer a very precise opinion which 22 scientists like to do. 23 Q. Okay. You cite I believe 24 the Heller study as evidence that talc</p>

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<p>1 does not have an inflammatory effect on 2 the ovaries, right? 3 A. I cite two studies. But one 4 of them is Heller, yes. 5 Q. Are you aware that Heller 6 only looked at one specimen out of 24 7 histologically? 8 A. I'd have to go back and look 9 at the paper again. 10 Q. If Heller only looked at one 11 specimen, would that be evidence of what 12 was in the other 23 specimens? 13 MS. SHARKO: Can we get a 14 copy of Heller? Please? 15 (Document marked for 16 identification as Exhibit 17 Neel-26.) 18 BY DR. THOMPSON: 19 Q. This will be Exhibit 26, 20 Heller paper, "The Relationship Between 21 Perineal Cosmetic Talc Usage and Ovarian 22 Talc Particles." 23 MS. SHARKO: Thank you. 24 BY DR. THOMPSON:</p>	<p>1 paper that they looked at any sections 2 using H&E light microscopy besides this 3 one -- 4 A. It's not clear from the way 5 this is written that that's the only -- 6 that they are saying that it -- from -- 7 that those are the only analyzed 8 sections. But, you know. 9 Q. But -- but you can conclude 10 from your reading of this that Heller 11 found no inflammatory reaction in the 12 ovaries of cells with -- of -- in the 13 ovaries of these subjects that they found 14 talc? 15 A. Well, they don't report on 16 it, so it's not evidence that there is 17 inflammation in the ovary. 18 Q. Well, you cited this paper, 19 right? 20 A. Yeah, I did cite to it -- 21 Q. For that purpose? 22 A. Yeah. I said that there was 23 no evidence. 24 Q. And you'll agree that there</p>
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<p>1 Q. And I'm looking at the last 2 paragraph of the results section, 3 Dr. Neel. 4 And it says, "In one subject 5 we studied both ovaries. On the right 6 side we detected no talc. On the left 7 side" -- "by electron microscopy and 556 8 particles by light microscopy. And on 9 the left side we detected 1,669,000 10 particles per gram of wet weight by 11 electron microscopy and six particles by 12 light microscopy. 13 "Hematoxylin and Eosin 14 stained slides from the analyzed sections 15 of tissues were examined. There was no 16 evidence of response to talc such as 17 foreign body giant cell reactions or 18 fibrosis in the tissue." 19 A. It's -- I mean, it's not 20 clear to me whether they only looked at 21 those, at the sections from the -- the 22 one subject above or not. Or whether 23 they looked at all of them. 24 Q. Do you see anywhere in the</p>	<p>1 is no evidence of more than one being 2 looked at, right? 3 A. As I said, I can't tell from 4 the way that's written whether it was all 5 of them or not. The major point for 6 citing this was that there was no 7 correlation between reported perineal 8 talc use and the presence of particles 9 assumed to be or -- or argued to be talc 10 in the ovaries. That was the major 11 reason for citing it. 12 Q. While we are on -- 13 A. We already have direct 14 evidence on the animal studies about what 15 talc does in ovaries. 16 Q. You cited the paper. 17 A. I did and I said -- 18 Q. Okay. 19 A. -- that they argued strongly 20 that perineal talc use does not 21 accurately reflect potential exposure. 22 And I stand by that statement. That's 23 exactly what the paper concludes. 24 Q. While we are on the Heller</p>

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<p>1 paper.</p> <p>2 Do you intend to give</p> <p>3 opinions as to whether perineal talc</p> <p>4 powder can migrate or be transported to</p> <p>5 the distal fallopian tube, ovary or</p> <p>6 perineal cavity?</p> <p>7 A. I intend to say that the</p> <p>8 evidence is inconclusive.</p> <p>9 Q. So you will say -- you will</p> <p>10 say that there is evidence on both sides?</p> <p>11 A. I say the preponderance of</p> <p>12 the evidence is negative.</p> <p>13 Q. What do you use for the</p> <p>14 preponderance of the evidence being</p> <p>15 negative?</p> <p>16 A. The best -- the best study</p> <p>17 is one that was done in monkeys by</p> <p>18 Whelan. All of the other studies are</p> <p>19 potentially confounded by artifact.</p> <p>20 Q. Is -- is it plausible that</p> <p>21 talcum powders -- talcum powder applied</p> <p>22 to the perineum can reach the fallopian</p> <p>23 tube, ovary and perineal cavity?</p> <p>24 A. Is it plausible? I think</p>	<p>1 there exists.</p> <p>2 "While there exists no</p> <p>3 direct proof of talc and ovarian</p> <p>4 carcinogenesis, the potential for</p> <p>5 particulates to migrate from the perineum</p> <p>6 and vagina to the perineal cavity is</p> <p>7 indisputable. It is, therefore,</p> <p>8 plausible that perineal talc and other</p> <p>9 particulate that reach the endometrial</p> <p>10 cavity, fallopian tubes, ovaries and</p> <p>11 peritoneum may elicit a foreign body type</p> <p>12 reaction and inflammatory response that</p> <p>13 in some exposed women may progress to</p> <p>14 epithelial cancers.</p> <p>15 "However, there was no</p> <p>16 conclusive evidence to support</p> <p>17 causality."</p> <p>18 MS. SHARKO: There has been.</p> <p>19 DR. THOMPSON: "Has been no</p> <p>20 conclusive evidence to support</p> <p>21 causality."</p> <p>22 BY DR. THOMPSON:</p> <p>23 Q. So even though the FDA</p> <p>24 determined that the potential for the</p>
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<p>1 it's unresolved. I can't say it's</p> <p>2 plausible or implausible. It's</p> <p>3 unresolved. It's -- it's unresolved.</p> <p>4 The strongest evidence says no.</p> <p>5 Q. And you cite as -- the -- as</p> <p>6 part of your opinions, this FDA citizen's</p> <p>7 response letter, correct?</p> <p>8 A. Mm-hmm.</p> <p>9 Q. And it's marked as exhibit</p> <p>10 something.</p> <p>11 I didn't write it on the</p> <p>12 thing.</p> <p>13 If you go to the --</p> <p>14 MS. SHARKO: Go to exhibit</p> <p>15 something?</p> <p>16 BY DR. THOMPSON:</p> <p>17 Q. Give it -- go to exhibit</p> <p>18 something and we'll take a break after.</p> <p>19 MR. ZELLERS: It's 18.</p> <p>20 DR. THOMPSON: Exhibit 18.</p> <p>21 Thank you, Mr. Zeller.</p> <p>22 BY DR. THOMPSON:</p> <p>23 Q. And on Page 5, I'm reading</p> <p>24 the paragraph that starts with while</p>	<p>1 particulates to migrate is indisputable,</p> <p>2 you're still saying that the</p> <p>3 preponderance of the evidence based on</p> <p>4 one monkey study is against it?</p> <p>5 A. Well, it's not one monkey</p> <p>6 study, first of all. It's two monkey</p> <p>7 studies. And one --</p> <p>8 Q. But by the same -- by the</p> <p>9 same Johnson & Johnson consultant, right?</p> <p>10 A. He's -- I don't know that</p> <p>11 they're a Johnson & Johnson consultant.</p> <p>12 Q. Did you look at the conflict</p> <p>13 of interest disclosure?</p> <p>14 A. No, I didn't. But it's --</p> <p>15 the study was done in the more accurate</p> <p>16 way than the other two studies. And it</p> <p>17 actually produced very clear evidence of</p> <p>18 potential confounding artifact in the --</p> <p>19 in the studies that have been done</p> <p>20 before.</p> <p>21 Q. So --</p> <p>22 MS. SHARKO: Wait. Let him</p> <p>23 finish.</p> <p>24 THE WITNESS: So the fact is</p>

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<p>1 that one very well-designed study</p> <p>2 beats multiple poorly designed</p> <p>3 studies in science. It's not a</p> <p>4 plebiscite.</p> <p>5 BY DR. THOMPSON:</p> <p>6 Q. You're saying that two</p> <p>7 monkey studies by a Johnson & Johnson</p> <p>8 consultant outweigh a vast body of</p> <p>9 literature on various substances,</p> <p>10 including particulates being transported,</p> <p>11 migrating to the ovaries, to reach your</p> <p>12 conclusion that the preponderance of the</p> <p>13 evidence is against migration or</p> <p>14 transport to particles?</p> <p>15 MS. SHARKO: I object to the</p> <p>16 form of the question. Lacks</p> <p>17 foundation.</p> <p>18 THE WITNESS: You haven't</p> <p>19 provided me with any -- vast</p> <p>20 literature? You provided me with</p> <p>21 two poorly designed studies. So I</p> <p>22 don't know what you're talking</p> <p>23 about. If you want to show me</p> <p>24 other studies, I'll be happy to</p>	<p>1 know of something that I don't know. But</p> <p>2 what I'm saying is this -- this --</p> <p>3 this -- you can't just make a statement</p> <p>4 without referencing it and then assume</p> <p>5 that -- and assume that scientists are</p> <p>6 going to take it at face value. We have</p> <p>7 to see the evidence. That's what we work</p> <p>8 with, evidence.</p> <p>9 Q. You really need evidence to</p> <p>10 show that something can go from the</p> <p>11 perineum through the genital tract?</p> <p>12 A. Well, sperm can go there.</p> <p>13 But they have -- but they have, you know,</p> <p>14 flagella. I'm not aware of talc having</p> <p>15 flagella.</p> <p>16 Q. Okay. Are you aware of the</p> <p>17 sperm studies that show dead sperm and</p> <p>18 sperm particles can migrate through the</p> <p>19 genital tract?</p> <p>20 A. I don't know what studies</p> <p>21 you are talking about. But if you want</p> <p>22 to give me studies --</p> <p>23 Q. Okay. Let me get them.</p> <p>24 A. -- I'll be happy to look at</p>
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<p>1 read them and give my opinion on</p> <p>2 them.</p> <p>3 However, it is well known</p> <p>4 that particle -- that radioactive,</p> <p>5 you know, materials can leach off</p> <p>6 of albumin particles. And also</p> <p>7 the study showing that carbon</p> <p>8 black is present -- it is true</p> <p>9 that the Egli study did not use --</p> <p>10 did not do a control where they</p> <p>11 just used the solutions</p> <p>12 themselves.</p> <p>13 So again the point raised by</p> <p>14 Whelan is a reasonable point,</p> <p>15 whether he's a consultant for</p> <p>16 Johnson & Johnson or not. Science</p> <p>17 is science. It doesn't matter who</p> <p>18 does it.</p> <p>19 BY DR. THOMPSON:</p> <p>20 Q. Are the FDA not scientists</p> <p>21 that say it's indisputable?</p> <p>22 A. I don't know what -- the FDA</p> <p>23 doesn't reference anything here, so I</p> <p>24 can't comment on the studies. Maybe they</p>	<p>1 studies and --</p> <p>2 Q. We'll take a break and get</p> <p>3 them.</p> <p>4 A. -- see if I think they are</p> <p>5 reliable.</p> <p>6 Q. Okay. We'll take a break</p> <p>7 and come back and go through the studies.</p> <p>8 THE VIDEOGRAPHER: The time</p> <p>9 is 2:10 p.m. Off the record.</p> <p>10 (Short break.)</p> <p>11 THE VIDEOGRAPHER: We are</p> <p>12 back on the record. The time is</p> <p>13 2:28 p.m.</p> <p>14 BY DR. THOMPSON:</p> <p>15 Q. Dr. Neel, has your research</p> <p>16 over the last 30 years -- plus years, had</p> <p>17 anything at all to do with the physiology</p> <p>18 of the female genital tract?</p> <p>19 A. No.</p> <p>20 Q. Have you written any papers</p> <p>21 that have anything to do with the</p> <p>22 physiology of the female genital tract?</p> <p>23 A. No.</p> <p>24 Q. Prior to being contacted by</p>

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<p style="text-align: right;">Page 278</p> <p>1 the lawyers in this case, did you have 2 any knowledge of the literature regarding 3 the potential migration or transport of 4 particles through the female genital 5 tract? 6 A. Only sperm. 7 Q. Only? 8 A. Only sperm. 9 Q. Only sperm. And were you 10 aware of the literature regarding sperm 11 particles or dead sperm being transported 12 through the genital tract? 13 A. No. 14 Q. Were you aware of the 15 literature that sperm moved more quickly 16 through the genital tract than would be 17 expected just from the motility of the 18 flagella? 19 A. I'm not aware of any studies 20 on that issue. 21 Q. Did you have any knowledge 22 of the concept of the uterine peristaltic 23 pump, which actually facilitates the 24 migration or transport of particles?</p>	<p style="text-align: right;">Page 280</p> <p>1 A. I think anybody who has gone 2 to medical school is pretty familiar with 3 the general anatomy of the genital tract. 4 Q. You don't think 5 gynecologists have a more in-depth 6 understanding of anatomy than other 7 non-GYN doctors? 8 A. I think they do have a more 9 detailed understanding of anatomy. That 10 doesn't necessarily mean they have a more 11 detailed understanding of anatomy that is 12 necessary to make a conclusion about 13 particles moving through the genital 14 tract. That doesn't require a very 15 complex surgical description of the 16 genital tract. 17 Q. Do they have more 18 understanding of the physiology of the 19 reproductive tract? 20 A. I would hope so, yeah. 21 Q. Let's go to the Taher 22 article. That would be Exhibit -- 23 A. 20. 24 MS. SHARKO: 20.</p>
<p style="text-align: right;">Page 279</p> <p>1 A. Not that I recall. 2 Q. Would you agree that a 3 gynecologist or GYN oncologist would have 4 a greater understanding of the migration 5 or transport of particles through the 6 genital tract? 7 A. They might have a greater 8 understanding of what's published in 9 textbooks, but they wouldn't necessarily 10 be any better than I am at evaluating 11 literature on the subject. 12 Q. But they would have more 13 firsthand knowledge and experience -- 14 A. As I said. 15 Q. -- in their practice, 16 wouldn't they? 17 A. I don't think the practice 18 of gynecological oncology addresses the 19 issue of the migration of particles 20 through the genital tract. So I don't 21 think so necessarily, no. 22 Q. They would be more familiar 23 with the anatomy of the genital tract, 24 right?</p>	<p style="text-align: right;">Page 281</p> <p>1 BY DR. THOMPSON: 2 Q. 20. And this -- this is the 3 article that you were referring to in 4 your report when you referenced Health 5 Canada, right? 6 A. Yes. And now I -- now I 7 recall where my statement came from in my 8 report. 9 So if you look at the bottom 10 of Page 1, it says, "For information 11 contact Dr. Donald R. Mattison." It has 12 his contact information. And it says, 13 "Materials submitted to Health Canada." 14 So that was where I got the 15 information that this was commissioned by 16 Health Canada. I may have misinterpreted 17 that. But that's where I got the 18 information from. And I think there's an 19 allusion to that also in the end. But 20 I'd have to look through it. If you want 21 me to, I will. 22 Q. Let's go to the chart on 23 Page 26. And -- 24 A. Hold on. I'm not there yet.</p>

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<p>1 That in the middle of a chart. It's the 2 middle of the chart. Do you want to 3 just -- 4 Q. 26. 5 A. -- on Page 26. 6 Q. I want to look at the -- 7 A. It continues on three pages. 8 Q. Yeah, I want to look at the 9 biological plausibility -- 10 A. Okay. 11 Q. -- section of the chart on 12 Page 26. 13 And this Taher article 14 states, under biological plausibility, 15 "Particles of" -- "of talc appear to 16 migrate into the pelvis and ovarian 17 tissue causing irritation and 18 inflammation." 19 Do you agree that that's a 20 biologically plausible mechanism? 21 A. If the data supporting it 22 were convincing, or even close to 23 convincing, yes. But they are not. 24 And so I agree that</p>	<p>1 A. So actually, if you look at 2 the report somewhere else, it says that 3 data on talc migration are inconsistent. 4 So we'll have to go through the entire 5 report to find that sentence. 6 But I don't think that you 7 should take this chart or this table and 8 state that as what the conclusion of the 9 report is because it's out of context. 10 Q. Well, this is Dr. Taher's 11 chart that is titled "Summary of 12 Evidence." 13 A. Well, Dr. Taher also wrote 14 that data on talc migration were 15 inconsistent. So we can look through it 16 and find out where that is, but I 17 wouldn't put that in my report unless I 18 saw it in this paper. 19 And Dr. Taher, I believe, is 20 an epidemiologist. So he -- he's not 21 really qualified to comment on biological 22 plausibility based on cellular mechanisms 23 anyway. 24 Q. So in your opinion, an</p>
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<p>1 conceptually that would be a reasonable 2 mechanism. But they don't have -- the -- 3 the actual studies are poor or 4 nonexistent in terms of evidence. 5 Q. So your opinion, with that 6 first statement, is you would need 7 convincing evidence to have that be a 8 biologically plausible mechanism? 9 A. I would need some 10 scientifically credible evidence. All of 11 the publications that I have -- that I 12 have found that address this issue, and 13 I'm happy to review other ones with you, 14 all of the ones that I've found are 15 really poor or they don't say that this 16 is true. 17 Q. The second one, bullet point 18 under biologically -- biological 19 plausibility says, "Transport of talc via 20 perineal stroma and presence in ovaries 21 documented." 22 Do you agree that that is a 23 biologically plausible part of the 24 mechanism?</p>	<p>1 epidemiologist is not qualified to 2 testify as to cellular mechanisms? 3 A. Unless they are trained in 4 cellular molecular biology as well, no. 5 Q. Okay. Do you disagree with 6 the authors of the Taher paper? 7 A. What -- which parts of the 8 authors they state in these statements? 9 Q. In this biological 10 plausibility section. 11 A. I think that, yes, I do 12 disagree with several of the statements 13 in the biological plausibility section. 14 Including the particles of talc appear to 15 migrate to the pelvis and ovarian tissue, 16 I think that remains unclear. 17 The fact that they cause 18 irritation and inflammation. Particles 19 of talc cause granulomas. There's no -- 20 I don't know what irritation means. 21 That's not a scientific term as you know. 22 And transport of talc via 23 perineal stroma. I don't really know 24 what perineal stroma means. Stroma</p>

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<p>1 actually is something that is 2 subepithelial, so I don't know what that 3 refers to. It's probably a misprint. 4 And presence in the ovaries 5 documented. We've already discussed 6 presence in the ovaries. But we haven't 7 established that that is from transport. 8 Q. Could -- could evidence be 9 inconclusive and both sides be plausible 10 in your mind? 11 A. Can evidence be inconclusive 12 and plausible at the same time? No. 13 Q. So if you have differing 14 evidence on an issue, neither one could 15 be plausible, is that your opinion? 16 A. No. Good evidence is 17 plausible. Bad evidence is not. It's 18 not a plebiscite. It's not an election. 19 It's not like you get a bunch of people 20 on one side and a bunch of people on the 21 other, and you take testimony and -- and 22 you tally up who gets what. 23 It's which evidence is 24 plausible scientifically and that has to</p>	<p>1 Science, Engineering, Medicine, and 2 supported by the CDC, that was a book 3 actually titled "Ovarian Cancer: 4 Evolving paradigms in research and care." 5 Correct? Do you remember 6 that? 7 A. You'll have to show -- 8 MS. SHARKO: Object to the 9 form of the question. 10 THE WITNESS: I said I had 11 seen several, you know, summary 12 reviews. 13 You'd have to show me the 14 exact. 15 BY DR. THOMPSON: 16 Q. I will. I just -- I had 17 remembered this morning that you were 18 aware that this had been published. But 19 I'm going to show it to you regardless. 20 (Whereupon, a discussion was 21 held off the record.) 22 DR. THOMPSON: 27. 23 Exhibit 27 will be "Ovarian 24 Cancer: Evolving paradigms in</p>
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<p>1 do with the quality of the data and the 2 convincingness of the evidence. And 3 that's not a plebiscite. 4 Q. So -- so you don't see a 5 situation where the evidence could be 6 credible on both sides of a scientific 7 question? 8 A. If two people do the same 9 experiment and they get different 10 results, and neither one -- and there -- 11 if two people do the same experiment and 12 they get different results, one of them 13 is right and one of them is wrong. 14 That's the essence of 15 science. It's empirically observable and 16 reproducible. So that's my opinion. 17 Q. So science is either right 18 or wrong? 19 A. Or good or bad. Yes. 20 Science is either right or 21 wrong by definition. 22 Q. You mentioned earlier that 23 you are at least aware of the treatise 24 commissioned by the National Academies of</p>	<p>1 research and care." 2 (Document marked for 3 identification as Exhibit 4 Neel-27.) 5 BY DR. THOMPSON: 6 Q. I did not print the whole 7 book. I did print the entire chapter 8 that I'm going to be referencing. 9 And -- 10 MR. ZELLERS: Margaret, do 11 you have one more of them? 12 DR. THOMPSON: I don't. I 13 just -- oh, I do. I'm sorry. 14 MS. SHARKO: Do you have a 15 paperclip? May I have that 16 paperclip? 17 DR. THOMPSON: You are so 18 demanding. 19 MS. SHARKO: Thank you. 20 BY DR. THOMPSON: 21 Q. And on page little Roman 22 numeral ix preface, "This congressionally 23 mandated report sponsored by the Centers 24 for Disease Control and Prevention</p>

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<p>1 assesses the state of research on ovarian 2 cancers from multiple perspectives and by 3 multiple disciplines." 4 Did I read that right, the 5 first sentence of -- 6 A. Yeah. 7 Q. -- of -- 8 A. I have not seen this report 9 before, so -- 10 Q. Okay. 11 A. -- just so you know. 12 Q. And this paper -- or this 13 book actually, was authored by a 14 committee of -- approximately 15 authors, 15 correct? 16 A. Yes. 17 Q. And this book also was 18 reviewed by another, it looks like ten or 19 so reviewers, correct? 20 A. Yes. 21 MS. SHARKO: Just for the 22 record, we don't have a book in 23 front of us. We have -- 24 DR. THOMPSON: Okay. The</p>	<p>1 It's an observation. 2 DR. THOMPSON: Well, we 3 don't need your speaking 4 observation. Dr. Neel can -- can 5 let me know if he needs time to 6 look at whatever it is I'm showing 7 him. 8 BY DR. THOMPSON: 9 Q. Dr. Neel, this section on 10 Page 110 titled "Inflammation" is under 11 the heading behavioral and inflammatory 12 risk factors. 13 And I'm going to read the 14 first part of this paragraph. "Studies 15 of the inflammatory marker C-reactive 16 protein suggest a possible association 17 between inflammation and an increased 18 risk of ovarian cancer." There are two 19 cites. 20 "Other specific inflammatory 21 factors have also been associated with 22 ovarian cancer. A meta-analysis reported 23 that exposure to asbestos was associated 24 with a 77 percent increased risk of</p>
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<p>1 chapter from the book. 2 MS. SHARKO: Okay. Thank 3 you. 4 BY DR. THOMPSON: 5 Q. Let's go to -- and this, the 6 chapter that I did take from this book is 7 titled "Prevention and Early Detection." 8 And if you'll go to 9 Page 110. The topic heading -- 10 A. Okay. I see the numbers 11 now. 12 MS. SHARKO: And the witness 13 should have the opportunity -- 14 DR. THOMPSON: Susan, we 15 don't need any speaking 16 objections. How many times do we 17 need to tell you that? 18 MS. SHARKO: Well, I'll 19 ignore -- 20 DR. THOMPSON: And there -- 21 the witness is perfectly -- 22 MS. SHARKO: I'll ignore 23 your rudeness. It's not an -- 24 it's not -- it's not an objection.</p>	<p>1 ovarian cancer mortality," citing 2 Camargo, "and the International Agency 3 for Research on Cancer determined that 4 there was sufficient evidence to support 5 a causal relationship between asbestos 6 exposure and ovarian cancer," citing 7 Straif. 8 "This has led to studies of 9 talc use, which is chemically similar to 10 asbestos and can cause an inflammatory 11 response. The use of talcum powder has 12 been associated with a 20 to 30 percent 13 increased risk of ovarian cancer, 14 although it has been shown" -- "show to 15 vary by histologic subtype." 16 Did I read that correctly? 17 MS. SHARKO: No. You left 18 out the word "perineal." 19 THE WITNESS: Yeah, perineal 20 talc. 21 BY DR. THOMPSON: 22 Q. Okay. Thank you. Anything 23 else? 24 A. I think you read that</p>

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<p style="text-align: right;">Page 294</p> <p>1 correctly.</p> <p>2 Q. Okay. So the state of the</p> <p>3 art committee that was commissioned by</p> <p>4 the National Academy of Science</p> <p>5 Medicine -- are you familiar with that</p> <p>6 organization?</p> <p>7 MR. LOCKE: Objection.</p> <p>8 THE WITNESS: Yes. I hope</p> <p>9 to be in it.</p> <p>10 What was that?</p> <p>11 MR. LOCKE: I just said</p> <p>12 objection.</p> <p>13 THE WITNESS: Okay.</p> <p>14 BY DR. THOMPSON:</p> <p>15 Q. And it has a reputation</p> <p>16 certainly, correct?</p> <p>17 A. Yes. I know most of the</p> <p>18 people on this panel.</p> <p>19 Q. Do you know -- do you know</p> <p>20 the authors?</p> <p>21 A. I know several of them.</p> <p>22 Q. Or the researchers?</p> <p>23 A. Several of them, yes.</p> <p>24 Q. And it's my understanding</p>	<p style="text-align: right;">Page 296</p> <p>1 ovarian cancer and that asbestos and</p> <p>2 talcum powder were associated with an</p> <p>3 increased risk; is that correct?</p> <p>4 MS. SHARKO: Objection to</p> <p>5 form. Lacks foundation.</p> <p>6 THE WITNESS: There are</p> <p>7 several questions there. Can you</p> <p>8 break them up?</p> <p>9 BY DR. THOMPSON:</p> <p>10 Q. Okay. These authors</p> <p>11 included inflammation under behavioral</p> <p>12 and inflammatory risk factors, correct?</p> <p>13 A. I think that you have to</p> <p>14 understand how to read the scientific</p> <p>15 literature. "Suggests a possible</p> <p>16 association" is a very weak statement.</p> <p>17 That means they suggest. That doesn't</p> <p>18 mean they establish. "Suggests a</p> <p>19 possible association between inflammation</p> <p>20 and increased risk of ovarian cancer."</p> <p>21 So no, it's not as strong as</p> <p>22 you made it out to be Number one.</p> <p>23 Number two is I've read the</p> <p>24 Poole, et al., paper and I have read the</p>
<p style="text-align: right;">Page 295</p> <p>1 that the authors of this treatise</p> <p>2 included not only GYN oncologists, but</p> <p>3 epidemiologists, molecular biologists,</p> <p>4 and others so that it would be a</p> <p>5 comprehensive report.</p> <p>6 A. Yes.</p> <p>7 Q. Is that your understanding</p> <p>8 as well?</p> <p>9 A. Mm-hmm.</p> <p>10 MS. SHARKO: Object to the</p> <p>11 form.</p> <p>12 BY DR. THOMPSON:</p> <p>13 Q. And it was also meant to be</p> <p>14 a state of the science in ovarian cancer</p> <p>15 research treatise.</p> <p>16 And this was published in</p> <p>17 2016, I believe; is that right?</p> <p>18 A. I think so.</p> <p>19 MS. SHARKO: Object to the</p> <p>20 form.</p> <p>21 BY DR. THOMPSON:</p> <p>22 Q. So at least these</p> <p>23 researchers had the opinion that</p> <p>24 inflammation was a risk factor for</p>	<p style="text-align: right;">Page 297</p> <p>1 subsequent papers by Poole and others.</p> <p>2 And the association between inflammation</p> <p>3 and increased risk of ovarian cancer, it</p> <p>4 doesn't distinguish between whether the</p> <p>5 inflammation is a marker of existing</p> <p>6 ovarian cancer or the inflammation is a</p> <p>7 cause of cancer, which has been what we</p> <p>8 discussed all morning.</p> <p>9 So I don't really think that</p> <p>10 this statement is in any way</p> <p>11 contradictory to anything that I've said</p> <p>12 this morning.</p> <p>13 As to the statement about</p> <p>14 asbestos and ovarian cancer, I've already</p> <p>15 said that I don't really have an opinion.</p> <p>16 I haven't had time or wasn't charged with</p> <p>17 doing an extensive analysis of ovarian</p> <p>18 cancer and asbestos.</p> <p>19 So I really don't think that</p> <p>20 I should comment on this statement. But</p> <p>21 it doesn't really review the evidence.</p> <p>22 Just to be -- just to point out that this</p> <p>23 statement does not review the evidence,</p> <p>24 it simply cites previous conclusions. So</p>

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<p>1 it really doesn't analyze the case any 2 more than those original papers did. 3 As for the statement of 4 talc, it cites, you know -- it cites two 5 studies that are, again, I think, both 6 case-control studies. It does not in any 7 way comprehensively review the 8 literature, and it says it's been 9 associated with it. It doesn't say it's 10 a causal association, which I thought was 11 what we were going to be discussing here 12 today. 13 DR. THOMPSON: I'll object 14 as nonresponsive. 15 BY DR. THOMPSON: 16 Q. Because my question was, did 17 these authors include a section on 18 inflammation in this treatise? 19 A. They -- they included a 20 section, but as I said, the section says 21 there's a possible association between 22 inflammation and an increased risk of 23 ovarian cancer. 24 Q. And if the authors didn't</p>	<p>1 There are a number of different 2 tumor types with characteristic 3 histologic features, distinctive 4 molecular signatures, and disease 5 trajectories." Moreover -- 6 MS. SHARKO: Slow. 7 THE WITNESS: "Moreover, 8 these tumors are heterogeneous and 9 they can arise from different 10 tissues of the female reproductive 11 tract." 12 So again, it just states 13 what I've been saying all day, is 14 that is that it's not meaningful 15 to talk about ovarian cancer as a 16 single entity. You have to break 17 it down into each of the diseases. 18 DR. THOMPSON: And that was 19 nonresponsive, because there was 20 not a question about asking 21 anything to do with that. 22 MS. SHARKO: Ignore that 23 comment and wait for the next 24 question.</p>
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<p>1 think it was plausible that that 2 association would be there, would they 3 have included it? 4 A. I don't presume to be in the 5 mind of the authors, and I don't know 6 which of the authors was the major author 7 of this section. So I can't answer that 8 question to any degree of certainty. 9 Can I point out one other 10 thing? 11 Q. I don't -- there's not a 12 question on the table. 13 MS. SHARKO: No, he's 14 finishing his answer. 15 THE WITNESS: I didn't 16 finish. 17 DR. THOMPSON: No, he's not. 18 MS. O'DELL: He is not. 19 THE WITNESS: I am. I meant 20 to point out that on Page 9, the 21 same preface that you only read a 22 small part of, at the bottom says, 23 "An overarching conclusion is that 24 ovarian cancer is not one disease.</p>	<p>1 DR. THOMPSON: Object as 2 nonresponsive. 3 BY DR. THOMPSON: 4 Q. Did you -- Dr. Neel, did you 5 review the literature on pleurodesis? 6 A. Not extensively, no. 7 Q. Was it not relevant, the 8 reaction in the tissue caused by talc 9 injected into the pleural space to 10 treat -- 11 A. It's relevant for the study 12 of mesothelioma. 13 Q. But it's not relevant for 14 the study of the inflammatory effect of 15 talc in the body? 16 A. It would be potentially 17 relevant to the studies of peritoneal 18 mesothelioma. But it's not necessarily 19 relevant to ovarian cancer, no. 20 Q. So it's your testimony that 21 injection of talcum powder into the 22 pleural space has no meaning at all for 23 what the reaction might be in a tissue 24 like the ovary?</p>

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<p>1 A. It has relevance to what --</p> <p>2 MR. LOCKE: Objection.</p> <p>3 THE WITNESS: Can I answer</p> <p>4 the question?</p> <p>5 MS. SHARKO: Yes.</p> <p>6 THE WITNESS: So it's --</p> <p>7 MS. SHARKO: You have to</p> <p>8 give everybody time to object.</p> <p>9 THE WITNESS: It has</p> <p>10 relevance to what the response of</p> <p>11 the mesothelial cells of the</p> <p>12 pleural cavity are. It might be</p> <p>13 somewhat relevant to the response</p> <p>14 of the pleural -- sorry the</p> <p>15 peritoneal mesothelial cells. But</p> <p>16 there are direct experiments that</p> <p>17 address, some of which we've</p> <p>18 discussed before, the effects of</p> <p>19 talc injections into the relevant</p> <p>20 tissues of ovarian cancer. So why</p> <p>21 would I look at the irrelevant</p> <p>22 tissues?</p> <p>23 BY DR. THOMPSON:</p> <p>24 Q. Because, do we have any</p>	<p>1 And also sort of the</p> <p>2 sentiment behind the FDA, and it's</p> <p>3 also what's listed on the NCI</p> <p>4 website.</p> <p>5 So I don't really think we</p> <p>6 should use the form -- the term</p> <p>7 "suggested carcinogen."</p> <p>8 That being said, no, it</p> <p>9 would not be ethical to do that</p> <p>10 study.</p> <p>11 BY DR. THOMPSON:</p> <p>12 Q. And if you had read that</p> <p>13 Health Canada assessment, you would know</p> <p>14 that Health Canada actually does suggest</p> <p>15 a causal association?</p> <p>16 MS. SHARKO: Object.</p> <p>17 MR. LOCKE: Objection.</p> <p>18 MS. SHARKO: Object to the</p> <p>19 form. Lacks foundation.</p> <p>20 Misstates the evidence.</p> <p>21 THE WITNESS: I'm happy to</p> <p>22 look over the thing and discuss it</p> <p>23 with you, but I did read the</p> <p>24 Taher, et al., paper, and the</p>
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<p>1 studies of injecting talcum powder into a</p> <p>2 woman's ovaries?</p> <p>3 A. Into female -- into actual</p> <p>4 females?</p> <p>5 Q. Yes.</p> <p>6 A. Not that I'm aware of.</p> <p>7 Q. Would it be ethical to</p> <p>8 inject a suspected carcinogen into a</p> <p>9 woman's ovaries?</p> <p>10 A. Well, I --</p> <p>11 MS. SHARKO: Object to the</p> <p>12 form of the question. Lacks</p> <p>13 foundation.</p> <p>14 THE WITNESS: First of all,</p> <p>15 I categorically deny that it's a</p> <p>16 suspected carcinogen. It's</p> <p>17 characterized as a possible</p> <p>18 carcinogen. And that has been the</p> <p>19 standard -- that has been the</p> <p>20 conclusion, not just of IARC but</p> <p>21 also of the -- of the Taher, et</p> <p>22 al., report. So I assume that's</p> <p>23 what Health Canada will end up</p> <p>24 saying.</p>	<p>1 Taher, et al., paper says the</p> <p>2 same -- basically the same thing</p> <p>3 as IARC: Possible.</p> <p>4 BY DR. THOMPSON:</p> <p>5 Q. And -- I'll leave it at</p> <p>6 that.</p> <p>7 (Document marked for</p> <p>8 identification as Exhibit</p> <p>9 Neel-28.)</p> <p>10 DR. THOMPSON: I'm going to</p> <p>11 mark this next article as</p> <p>12 Exhibit 28. And I just -- oh, I</p> <p>13 do have two.</p> <p>14 MS. SHARKO: Thank you.</p> <p>15 BY DR. THOMPSON:</p> <p>16 Q. The correspondence that I'm</p> <p>17 interested in having you discuss with me</p> <p>18 is on the second page, "Talcum should not</p> <p>19 be used for pleurodesis with nonmalignant</p> <p>20 pleural effusions."</p> <p>21 And I'll give you a chance</p> <p>22 to look at that if you'd like.</p> <p>23 A. Yeah. So that is these</p> <p>24 people's opinion.</p>

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<p>1 Q. I agree. But at least these 2 scientists felt strongly that talc should 3 not be used for pleurodesis, correct? 4 A. Apparently, yes. 5 Q. And they stated that "talc 6 is not a uniform substance and varies 7 significantly in size and chemical 8 composition with the latter depending on 9 geologic origin. This sheet silicate can 10 be contaminated with" -- "by asbestos, in 11 association between carcinogenesis and 12 exposure to asbestos included in talc, 13 appears credible." 14 Do you have an opinion 15 regarding that statement? 16 A. Yes. As I said, I think 17 that -- that my opinion, based on 18 everything that I've read is as I've 19 stated it in my report, which is that 20 there's no credible scientific evidence 21 that talc causes cancer in the female 22 genital tract. 23 So again, I don't really 24 think that this -- there's -- this is</p>	<p>1 A. That's what they said. But 2 I have nothing to say about that. As 3 I've said before. 4 Q. So you have no knowledge one 5 way or the other whether fibers occur in 6 talcum powder, and if so, whether there 7 would be any health hazard as a result? 8 A. I can only comment on the 9 studies that I read and commented on in 10 my report, which have to do with the use 11 of talc as cited in the methods and 12 materials sections of the epidemiology 13 studies and in the specific biological 14 experiments that I cited. 15 I am not a mineralogist. I 16 am not a geologist. I have no comment on 17 the composition of talc today or prior to 18 today, like in 2001, which was much long 19 ago. So I don't even know that it's 20 relevant to today. 21 Q. If you have a -- if you turn 22 to Page 25 of your report. And you are 23 discussing the Buz'Zard paper. And your 24 opinion is that "this study and its</p>
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<p>1 basically just citing a couple of papers, 2 and it's not in any way reputing anything 3 that I've said, so... 4 And I don't even know where 5 it's from. It's not cited on there. It 6 wasn't -- I don't -- 7 Q. It's not -- it's from the 8 American Journal of Respiratory -- 9 A. Yeah. 10 Q. -- and Critical Care 11 Medicine, 2001. 12 A. Which, again, this was in 13 2001. There's a lot of science since 14 2001. I don't think it's relevant. 15 And furthermore it's not 16 peer reviewed. 17 So I don't think it's 18 relevant. 19 Q. And that's fine. But I am 20 still entitled to ask you about it. 21 The authors at least were 22 concerned about the presence of fibers, 23 talc fibers in talcum powder used for 24 pleurodesis, correct?</p>	<p>1 interpretation by plaintiffs' experts is 2 seriously flawed for multiple reasons." 3 The first reason that you 4 give is, "The -- "the talc was obtained 5 from a standard chemical reagent company, 6 Sigma, and its quality, mineral and/or 7 fibrous content and composition were not 8 assessed." 9 A. Mm-hmm. 10 Q. And that was a criticism of 11 the Buz'Zard paper, correct? 12 A. Yes. Correct. 13 Q. Do you know anything 14 whatsoever about the quality, mineral 15 and/or fibrous content and composition of 16 Johnson's Baby Powder? 17 A. No. But I know that -- that 18 this study just used Sigma talc. So it's 19 not directly relevant to Johnson & 20 Johnson's products. That was my point in 21 that statement. 22 Q. So studies done with talcum 23 powder would not be relevant to Johnson's 24 Baby Powder?</p>

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<p>1 A. Studies done with talcum 2 powder would not be directly relevant to 3 Johnson' Baby Powder, but studies done 4 with Johnson & Johnson Baby Powder are 5 relevant. So...</p> <p>6 But in any event, this paper 7 is not conclusive in any way that talc is 8 pro-oncogenic.</p> <p>9 Q. I -- I didn't ask that 10 question. That's nonresponsive. 11 I was just asking why it 12 mattered what the quality, mineral, 13 and/or fibrous content and composition 14 were in the paper using talcum powder by 15 Buz'Zard.</p> <p>16 MS. SHARKO: Is that -- 17 wait. Is that a question? Or is 18 that an explanation for why you 19 asked the question?</p> <p>20 BY DR. THOMPSON: 21 Q. Does it matter what the 22 quality, mineral and/or fibrous content 23 and composition of talcum powder is when 24 you're assessing its potential molecular</p>	<p>1 in this litigation. 2 You said prior to this 3 litigation, didn't you? 4 Q. I did. 5 Did you look at Dr. Saed's 6 CV after being retained to testify in 7 this litigation? 8 A. I -- I didn't look. I don't 9 recall if I looked at his complete -- I 10 think I did look at his CV in the context 11 of his report. But I also did a search 12 on PubMed for the relevant papers. 13 Q. That was Exhibit 29. A 14 partial -- 15 (Document marked for 16 identification as Exhibit 17 Neel-29.) 18 MS. SHARKO: This begins 19 with Page 29? 20 DR. THOMPSON: Yes. 21 MS. SHARKO: Is that 22 correct? 23 DR. THOMPSON: Yes. 24 BY DR. THOMPSON:</p>
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<p>1 effects? 2 MS. SHARKO: Objection. 3 Asked and answered. 4 THE WITNESS: It matters if 5 you are trying to infer from 6 studies done with Sigma that that 7 definitely applies to Johnson & 8 Johnson's products. 9 But in this case, because 10 the evidence doesn't really say 11 anything that's relevant, it 12 doesn't matter. 13 BY DR. THOMPSON: 14 Q. You are very critical of 15 Dr. Saed's work, correct? 16 A. Yes. 17 Q. Did you look at Dr. Saed's 18 CV prior to this litigation? 19 A. No. 20 Q. Would that be something that 21 you would be interested in, as to what 22 Dr. Saed has published previously? 23 A. Oh, I looked at his 24 publications subsequent to being engaged</p>	<p>1 Q. And like -- like yourself, 2 Dr. Saed's CV is quite extensive. 3 A. I wouldn't agree with that 4 statement. 5 Q. Okay. It's 100, over 100 6 pages. So -- 7 A. Quantity is not quality. 8 Q. I -- 9 A. It's voluminous, but it's 10 not published in highly cited journals, 11 and I'm sure his H index is quite low. 12 Q. I didn't ask any question 13 about where it was -- 14 A. Yes, you did. 15 Q. -- where it was published 16 or -- I just -- 17 A. Well, that's quite relevant. 18 MS. SHARKO: All right. 19 What's the next question? 20 DR. THOMPSON: Well, if you 21 let me ask it, I will. 22 MS. SHARKO: Thank you. 23 BY DR. THOMPSON: 24 Q. Did you consider Dr. Saed's</p>

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<p>1 CV important or Dr. Saed's previous 2 publications? 3 A. Once I read them, yes. I 4 didn't read all of them. But I read 5 several of them, as I've cited in my 6 report. And I'm happy to go through each 7 one of them and show why they're all 8 flawed. 9 Q. I'm asking questions. 10 A. I'm answering your 11 questions. 12 Q. That's not something I want 13 to know. I don't believe I asked that 14 particular question. 15 A. You asked me if I considered 16 them relevant. And I told you that I 17 did. And I read them, and that's why I 18 assessed the studies as quite poor. 19 Q. Looking at his CV, would you 20 agree that the focus of his lab has the 21 study of oxidative stress and its 22 biological effects? 23 MS. SHARKO: We don't have 24 his CV in front of us.</p>	<p>1 epithelial ovarian cancer? 2 A. I don't know what "many 3 scientists" mean. Some scientists do. 4 Q. Some scientists? 5 A. Yes. 6 Q. Do you disagree with those 7 scientists? 8 A. I think that oxidative 9 stress resulting from follicular fluid 10 that's released from ovarian -- from 11 ovulation events, there could be 12 prooxidant species in there. But I 13 certainly think that oxidative stress 14 arising from general metabolism, which is 15 primarily endogenous, mitochondrial 16 oxygen -- the act of oxygen production 17 can contribute to cancer generation. 18 Q. And you do not believe that 19 oxidative stress from exogenous factors 20 plays a role? 21 A. I don't think there's any 22 compelling evidence that oxidative stress 23 from exogenous agents plays a role in 24 high grade serous ovarian cancer. That's</p>
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<p>1 BY DR. THOMPSON: 2 Q. Looking at his published 3 articles, would you agree that the focus 4 of his lab has been the study of 5 oxidative stress and its biological 6 effects? 7 A. Some of the papers are on 8 that. Some of them are on other things. 9 So, you know, one area of focus appears 10 to be on oxidative stress. 11 Q. What is oxidative stress? 12 A. So cells are exposed to -- 13 we live in an oxidative environment, as 14 we breathe oxygen. So we live in a 15 highly oxidative environment. And 16 proteins and other biomolecules, 17 including DNA, undergo oxidative events. 18 And oxidative stress occurs 19 when the pro-oxidative potential of cells 20 exceeds the antioxidant capacity of 21 cells. So that's oxidative stress. 22 Q. And is it fair to say that 23 many scientists believe that oxidative 24 stress plays a role in the etiology of</p>	<p>1 what I think. 2 I think that it's 3 conceivable, one of the possible 4 mechanisms by which obesity promotes 5 other forms of ovarian cancer, is 6 through -- indirectly through oxidative 7 stress, and there are several mechanisms 8 for that. 9 Q. Is a role that oxidative 10 stress plays in the pathogenesis of 11 cancer and ovarian cancer something that 12 would be considered controversial in the 13 scientific community, would you say? 14 A. I think it's open to 15 question, yes. I think -- yes. 16 Q. So there's some scientists 17 that believe that it does play a role and 18 others that believe -- who believe it 19 does not, correct? 20 A. Yes, but talking about 21 oxidative stress, you have to realize 22 it's -- to be meaningful, you have to 23 really narrow down what kind of sources 24 of oxidative stress we are talking about.</p>

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<p>1 Q. And is it your opinion that 2 oxidative stress from exogenous sources 3 has no role in ovarian cancer? 4 A. I think I just answered that 5 question. 6 Q. Okay. And do you believe 7 that the scientists that would take 8 another position are unreasonable? 9 A. I would have to see the 10 details of the position. My objection to 11 Dr. Saed's data, results or claims, are 12 not that he's taking another position. 13 It's that the evidence that he adduces to 14 support his claims is either nonexistent 15 or poor. 16 Q. But there are other 17 scientists that have reported similar 18 experiments and -- to Dr. Saed, and would 19 you include them in the same category? 20 A. You'll have to tell me 21 exactly what experiments you are 22 referring to. 23 Q. Okay. 24 A. I don't think anybody has</p>	<p>1 as nonresponsive. 2 BY DR. THOMPSON: 3 Q. I asked you for a paper. 4 A. Well, the paper -- the paper 5 is the TCGA report. And if you look at 6 the tables that come with the TCGA report 7 which are now put on websites, and it is 8 there. So yes, the TCGA 2012 report has 9 RNA sequencing data on ovarian cancers, 10 and if you look at that you will see that 11 there's no significant expression of 12 myeloperoxidase in ovarian cancer. 13 MS. SHARKO: Mr. Tisi, could 14 you -- it's happened several 15 times. Could you please not talk 16 while the witness is talking. 17 MR. TISI: Actually I don't 18 think -- I'd be curious if you 19 heard it. 20 THE WITNESS: I actually 21 did, but I tried to focus on DR. 22 THOMPSON. 23 MR. TISI: I'm allowed to 24 whisper to my colleague here. So</p>
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<p>1 reported the myeloperoxidase in ovarian 2 cancer cells because it doesn't appear to 3 be. So there's many statements, as I 4 pointed out in my report, that are 5 contradicted by other data in the 6 literature, including large scale studies 7 done by international groups to look at 8 ovarian cancer genetics. 9 Q. Can you direct me to a paper 10 that explicitly states that 11 myeloperoxidase does not occur in ovarian 12 cancer cells? 13 A. If you look on the website 14 that has all of the RNA sequencing data 15 from the TCGA, you can see as I showed 16 you in my report, that the level of 17 myeloperoxidase RNAs below the level of 18 action of tumor suppressing gene. So 19 that is data. 20 If you would like to look 21 through the tables of the TCGA report on 22 which that's based, you can find the 23 actual RNA sequence for myeloperoxidase. 24 DR. THOMPSON: Not -- object</p>	<p>1 if I interrupt you, I apologize. 2 Would you do me a favor and let me 3 know if -- 4 MS. SHARKO: No. His job 5 is -- his job is not to police 6 you, Mr. Tisi. 7 MR. TISI: Well, your job is 8 not to -- is not to school me, 9 Susan. So I apologize if he heard 10 me. And I leaned over and spoke 11 to my colleague here. So please 12 proceed. 13 DR. THOMPSON: We're going 14 to look at some of Dr. Saed's 15 other literature. 16 BY DR. THOMPSON: 17 Q. But I think there are 18 several papers regarding myeloperoxidase. 19 Those have all been peer-reviewed, the 20 ones that are published, correct? 21 MS. SHARKO: I object to the 22 form of the question. 23 BY DR. THOMPSON: 24 Q. Has Dr. Saed published</p>

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<p style="text-align: right;">Page 322</p> <p>1 papers regarding myeloperoxidase that 2 have been peer-reviewed? 3 A. Yes, he has. 4 Q. And there are other authors 5 on those papers as well, correct? 6 A. I think they are all from 7 his lab. 8 Q. Is there any overlap between 9 your research and phosphorylation 10 cascades and signal transduction -- did 11 I -- was that kind of close? 12 A. It's good. 13 Q. It worked. All right. 14 -- and Dr. Saed's research 15 in oxidative stress? 16 A. I'm an expert in oxidation 17 of protein-tyrosine phosphatases. We 18 developed some of the novel technologies 19 that were published in high quality 20 journals on this subject. So I do have, 21 you know, a significant familiarity with 22 the issues attended to oxidative stress 23 and oxidation-induced signaling. 24 So ox -- you know, reactive</p>	<p style="text-align: right;">Page 324</p> <p>1 exclusive -- 2 A. I don't -- 3 Q. -- to what you're working 4 on? 5 A. I know -- so my interest in 6 oxidation has to do with normal 7 physiological regulation and pathological 8 regulation of protein tyrosine 9 phosphatase activity. 10 I'm not sure which 11 particular paper of Dr. Saed you are 12 referring to, but I think many of the 13 papers don't address what you say they 14 are addressing. They may say that in the 15 title, but they don't address that issue. 16 Q. You would agree that 17 inflammation is part of a wider signaling 18 network, wouldn't you? 19 A. That inflammation is part of 20 a wider signaling network? No, I 21 wouldn't agree with that statement. I 22 don't see that that's-- 23 Q. Is -- is -- 24 A. -- it's a non sequitur in my</p>
<p style="text-align: right;">Page 323</p> <p>1 oxygen species are not just produced as a 2 pathological event. They're actually 3 part of normal growth factor and cytokine 4 signaling. And I've worked on the fact 5 that oxidative -- reactive oxygen species 6 react with the highly activated 7 neutrophilic cysteines, neutrophilic 8 cysteines of protein-tyrosine 9 phosphatases. And that's thought to be 10 part of normal signaling. That's the 11 only overlap. 12 Q. And I understand that you do 13 not accept Dr. Saed's research as 14 credible. But I'm trying to establish if 15 your work and his work are mutually 16 exclusive. Can both -- can -- are both 17 plausible mechanisms? 18 A. My work -- my -- well, you 19 haven't told me what mechanisms of 20 Dr. Saed you are talking about. 21 Q. Well, let's just say 22 oxidative stress and its role in the 23 pathogenesis of ovarian cancer. 24 Is that mutually</p>	<p style="text-align: right;">Page 325</p> <p>1 opinion. 2 Q. Is oxidative stress a part 3 of a wider signaling network in your 4 opinion? 5 A. What do you mean by 6 signaling network? I mean you're using, 7 you know, jargon that's not very 8 specific. 9 Q. Well, I probably read that 10 somewhere. 11 Are there researchers -- I'm 12 thinking particularly of Dr. Finkel? Do 13 you know Dr. Finkel? 14 A. Torin Finkel? Yes, I 15 know -- I don't know Torin Finkel 16 personally, but I know his work. 17 Q. Does Dr. Finkel study signal 18 transduction by reactive oxygen species? 19 A. Yes. His initial studies 20 were the ones that provided the first 21 evidence that normal react -- that 22 reactive oxygen species were produced in 23 response to normal growth factor 24 signaling. I think the original paper</p>

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<p style="text-align: right;">Page 326</p> <p>1 was on PDGF stimulation of smooth muscle 2 cells and the evidence was that blocking 3 oxidate with hydrogen peroxide generation 4 by smooth muscle cells impeded PDGF 5 receptor phosphorylation, which actually 6 got me interested in the field since the 7 most plausible mechanism by which that 8 might occur would be inhibition of 9 tyrosine phosphatase which we were 10 working on -- we and others subsequently 11 provided evidence to support that, as did 12 Finkel. 13 Q. And that would be intrinsic 14 ROS? 15 A. That would be -- 16 Q. Or -- 17 A. -- those would be -- that 18 would be intrinsically produced ROS in 19 response to growth factor signaling, not 20 through mitochondria probably, but 21 through a series of enzymes called NOXs 22 or NADPH oxidases. 23 Q. Do you agree that an 24 increase in ROS levels under certain</p>	<p style="text-align: right;">Page 328</p> <p>1 regarding oxidative stress and ovarian 2 cancer, correct? 3 MS. SHARKO: Wait. I -- I 4 object to the preface and the 5 speech and, therefore, the form of 6 the question. 7 What is the question you're 8 asking him? 9 BY DR. THOMPSON: 10 Q. Dr. Saed does not have 427 11 publications on oxidative stress and 12 cancer, does he? 13 A. Well, I don't think he has 14 427 publications. So I guess that means 15 he doesn't have 427 publications on 16 oxidative stress and cancer. 17 Q. So someone else is 18 publishing on oxidative stress and 19 ovarian cancer, correct? 20 A. I don't know. I haven't 21 done the specific search you did and I 22 haven't looked at the papers but I'm 23 happy to look at every single one of 24 them.</p>
<p style="text-align: right;">Page 327</p> <p>1 conditions can cause DNA mutations? 2 A. Yes. 3 Q. And cancer is the result of 4 genetic mutations, correct? 5 A. Yes. 6 Q. So under the right 7 conditions, chronic inflammation could 8 result in increasing ROS that could cause 9 genetic mutations that could cause 10 cancer, theoretically? 11 A. In certain context, yes. 12 Q. When I searched PubMed, I 13 found the following, searching cancer and 14 inflammation. 78,901, does that sound 15 reasonable? 16 A. I have no idea, but I 17 wouldn't -- 18 Q. Ovarian cancer and 19 inflammation, 1306. Oxidative stress and 20 cancer, 23,845 publications. And 21 oxidative stress and oxidative cancer, 22 427. 23 Dr. Saed doesn't have 24 anywhere close to 427 publications</p>	<p style="text-align: right;">Page 329</p> <p>1 And I'm not saying that 2 there is no possibility that oxidative 3 stress plays a role in ovarian cancer. 4 I'm saying Dr. Saed's papers are 5 categorically and fundamentally flawed in 6 almost every single instance. 7 Q. So are you saying that 8 oxidative stress is a plausible mechanism 9 for ovarian cancer? 10 A. I'm not taking a position 11 one way or the other on that issue. 12 Q. Okay. So you do not have 13 a -- you don't have a position on whether 14 oxidative stress has a role in the 15 pathogenesis of ovarian cancer. Your 16 opinions today are specifically about 17 Dr. Saed and his work? 18 MS. SHARKO: Object to the 19 form of the question. Lacks 20 foundation. 21 THE WITNESS: Can you ask 22 both questions separately? 23 BY DR. THOMPSON: 24 Q. Yeah.</p>

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<p style="text-align: right;">Page 330</p> <p>1 A. I categorically say that 2 none of Dr. Saed's work that was put 3 forward as evidence in support of his 4 contentions in his report is credible. 5 That I say categorically. 6 Q. Okay. 7 A. In terms of whether 8 oxidative stress plays a role in ovarian 9 cancer, that question is too broad. If 10 you narrow the question and ask me a more 11 specific question, I might be able to 12 give an opinion. But I think the issue 13 is still under debate. 14 I think I made it very clear 15 what the well-established pathogenesis of 16 ovarian cancer is. 17 There's -- there is one SNP 18 which I mentioned in my report, GPX-6, 19 which interestingly is not a SNP that 20 Dr. Saed cites, because I don't think 21 he's familiar with the GWAS literature. 22 That's the -- is associated. 23 I haven't had a chance to 24 really look in detail as to what's known</p>	<p style="text-align: right;">Page 332</p> <p>1 for publication. 2 But if you'd like me to look 3 at the final paper, I'm happy to do it. 4 I doubt that there's anything 5 different -- that's materially different 6 from what I wrote in my report. 7 Q. But you didn't see any 8 reason to look at it? 9 A. I didn't realize it was out 10 yet. 11 Q. And your attorneys didn't 12 provide the final published paper? 13 A. They mentioned to me 14 yesterday that the -- 15 MS. SHARKO: Well, wait, 16 wait. What was discussed with the 17 attorneys is privileged. 18 BY DR. THOMPSON: 19 Q. In your report you state 20 that Dr. Saed's work is "technically and 21 conceptually flawed and does not 22 withstand critical scrutiny." 23 Did you write that 24 statement?</p>
<p style="text-align: right;">Page 331</p> <p>1 about that SNP. So that SNP does raise 2 the possibility that oxidative stress in 3 some form might be involved in the 4 pathogenesis of some ovarian cancer. But 5 I haven't really studied that in detail. 6 BY DR. THOMPSON: 7 Q. In -- in your -- you have 8 not seen Dr. Saed's published paper, 9 correct? 10 A. I saw the manuscript that 11 was accepted for publication. 12 Q. But you don't know whether 13 that manuscript is the same as what was 14 actually published, correct? 15 A. Manuscripts accepted for the 16 publication in my 30 years of experience 17 as a faculty member are identical, except 18 for minor positioning of figures. 19 Q. Okay. So you've never made 20 edits on the final proof that's come back 21 to you? 22 A. If it's accepted for 23 publication, that's the final proof. 24 The -- the version that's marked accepted</p>	<p style="text-align: right;">Page 333</p> <p>1 A. Yes. Every word. 2 Q. Is that a statement that you 3 would put in a scholarly publication? 4 A. Technically and conceptually 5 flawed, yes. But it would be assumed if 6 I said that paper was -- in fact I've 7 used that phrase many times in reviews. 8 Well, sometimes I say technically flawed. 9 Sometimes I say conceptually flawed. And 10 when, as in the case of Dr. Saed's work, 11 it's both, I say conceptually and 12 technically flawed. That's exactly the 13 wording that I would use in reviews. 14 That being said, I would not 15 say that it wouldn't withstand scientific 16 scrutiny because it would be assumed and 17 understood by all scientists, including 18 editors of journals, that when I say 19 those statements that it doesn't 20 withstand scientific scrutiny. 21 Q. That paper was peer-reviewed 22 and accepted for publication and 23 published, correct? 24 A. At a very low impact</p>

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<p>1 journal, yes.</p> <p>2 Q. And did you review the peer</p> <p>3 reviewers' comments to Dr. Saed's paper?</p> <p>4 A. I did. I think I cited some</p> <p>5 of the peer reviewers' comments.</p> <p>6 Q. And we'll go over those in a</p> <p>7 minute.</p> <p>8 And did you also write the</p> <p>9 sentence that questioned Dr. Saed's,</p> <p>10 quote, knowledge of basic cancer cell</p> <p>11 biology, genetics and biochemistry?</p> <p>12 A. Yes, I did.</p> <p>13 Q. What was your basis of</p> <p>14 questioning his knowledge of basic cancer</p> <p>15 cell biology, genetics and biochemistry?</p> <p>16 A. Well, there were several</p> <p>17 reasons that I based that. So it had to</p> <p>18 do with the fact that, for example, he</p> <p>19 mischaracterized -- can we go to the</p> <p>20 actual page in my report? I think I</p> <p>21 actually provide the explanations there.</p> <p>22 Where is that exactly? Oh, okay here. I</p> <p>23 said it.</p> <p>24 Q. Page 23.</p>	<p>1 there?</p> <p>2 A. I don't know what</p> <p>3 literature -- p53 is the paradigmatic</p> <p>4 tumor suppressor gene along with RD and</p> <p>5 PTEN.</p> <p>6 Q. And you state one of your</p> <p>7 basis for that claim is that Dr. Saed</p> <p>8 makes a truly extraordinary claim that</p> <p>9 talc treatment was associated with a</p> <p>10 genotype switch for SNPs in redox</p> <p>11 enzymes. If you read his paper, it would</p> <p>12 be clear that he was talking about a</p> <p>13 nucleotide -- nucleotide switch, correct?</p> <p>14 A. That's what a genotype is.</p> <p>15 MR. LOCKE: Objection.</p> <p>16 BY DR. THOMPSON:</p> <p>17 Q. Well, why is that an</p> <p>18 extraordinary claim?</p> <p>19 A. Because it's impossible that</p> <p>20 that would happen in 72 hours in, in</p> <p>21 effect, a single nucleotide with</p> <p>22 100 percent penetrance.</p> <p>23 Q. So do you believe that</p> <p>24 Dr. Saed made up his results?</p>
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<p>1 A. Yes. Dr. Saed -- okay. For</p> <p>2 example, he states that p53 is an</p> <p>3 oncogene, whereas it is a paradigmatic</p> <p>4 tumor suppressor gene.</p> <p>5 He stated in his deposition</p> <p>6 that cells are grown at normal oxygen and</p> <p>7 glucose level.</p> <p>8 Q. And they --</p> <p>9 A. That's not true. I put the</p> <p>10 explanation.</p> <p>11 Q. I know. We're going to go</p> <p>12 over those now.</p> <p>13 A. I'm just answering your</p> <p>14 question.</p> <p>15 Q. For example, he states that</p> <p>16 p53 is an oncogene. Are you aware of</p> <p>17 literature that describes p53 as an</p> <p>18 oncogene?</p> <p>19 A. The lit -- p53 was</p> <p>20 originally described as an oncogene, and</p> <p>21 that was discovered subsequently that it</p> <p>22 was a tumor suppressor gene.</p> <p>23 Q. There is literature still</p> <p>24 that refers to p53 as an oncogene, isn't</p>	<p>1 A. I have no idea why Dr. Saed</p> <p>2 is making that claim. But it's simply</p> <p>3 impossible. It would be like finding a</p> <p>4 needle in a haystack and turning the</p> <p>5 needle into a hammer.</p> <p>6 Q. Did any of the peer</p> <p>7 reviewers say that that claim was</p> <p>8 extraordinary?</p> <p>9 A. I don't recall if they</p> <p>10 commented on it. I don't think they did,</p> <p>11 which illustrates the poor quality for</p> <p>12 peer review for that journal. There's no</p> <p>13 way that statement would have escaped the</p> <p>14 attention of any qualified peer reviewer.</p> <p>15 And I believe that if you</p> <p>16 read Dr. Birrer's report, he points to</p> <p>17 the same issue. So any qualified</p> <p>18 molecular biologist would have noted that</p> <p>19 and pointed out how absurd the claim.</p> <p>20 Q. Are you aware that the</p> <p>21 abstract that describes the mutations in</p> <p>22 the SNPs was reviewed by five to six</p> <p>23 reviewers and accepted for presentation</p> <p>24 at the SGO meeting?</p>

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<p>1 A. I have no idea who reviewed 2 those. But they also have no knowledge 3 of modern molecular biology if they 4 accepted that claim. The fact that they 5 don't understand what they're reviewing 6 doesn't mean that they know what they're 7 talking about. I'm telling you that 8 there is absolutely no way that you can 9 get that kind of a genotype. 10 In -- plus, I looked at the 11 underlying data on which he based his 12 claim, and the actual assay is flawed, 13 and he didn't do the follow-up study that 14 would have been necessary to prove that 15 it was true. 16 MS. SHARKO: I would just 17 ask that we be provided with a 18 copy of these five to six peer 19 reviewers. I think the court 20 ordered you to do that, and I'll 21 send you yet another letter on it. 22 But that doesn't sound like 23 something that was produced to us 24 among the peer review that was.</p>	<p>1 question. 2 Since, you know, Ms. Sharko 3 challenged me, you've been program 4 director for meetings, correct? 5 A. Yes. 6 Q. What was your policy or AACR 7 policy for evaluating and determining 8 what abstracts to accept for presentation 9 at a meeting, at a national meeting? 10 A. First of all, my 11 understanding was that this was not 12 presented. It was presented as a poster. 13 That's a big difference. 14 Q. Okay. Whatever the level, 15 poster, presentation, published abstract. 16 How did that process work when were you 17 program director? 18 A. So we had people reviewing 19 the abstracts. The reviews for 20 abstracts, especially those for poster -- 21 when you review abstracts at a meeting 22 like this, there's literally thousands of 23 abstracts. So you have to read through a 24 lot of them very quickly. And the</p>
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<p>1 And so, we'd like a copy. 2 DR. THOMPSON: There is 3 nothing in writing for abstracts 4 accepted for meetings. But I can 5 give you the policy of the meeting 6 regarding how abstracts are peer 7 reviewed. 8 MS. SHARKO: You just said 9 there were five to six peer 10 reviewers. Now you're saying 11 there aren't? 12 DR. THOMPSON: I said they 13 don't provide anything to the 14 authors of abstracts regarding the 15 results of their peer review. 16 THE WITNESS: Can I respond 17 to that? 18 BY DR. THOMPSON: 19 Q. I haven't asked you a 20 question. 21 MS. SHARKO: She's not going 22 to ask you the question. Sorry. 23 BY DR. THOMPSON: 24 Q. Sure. I'll ask you the</p>	<p>1 standard for accepting things for posters 2 is quite low. It's nowhere near rigorous 3 as what you would get for a high quality 4 journal. 5 And Basically, people just 6 want to see what's in the poster. 7 So the fact that it was 8 passed -- that five people looked at it 9 means that it was probably written in 10 English, and not much more. 11 Q. And if SGO accepts 12 25 percent of abstracts submitted, that 13 would probably be typical for a large 14 national meeting? 15 A. No. Not for posters. I 16 think when I was AACR program director, 17 we accepted a lot more than that. And 18 from other meetings, like Cold Spring 19 Harbor meetings and facet (ph) meetings, 20 we accept all the poster abstracts. It's 21 the presented ones, the ones that are 22 plenary sessions that are given as oral 23 presentations, those are the ones that 24 get a little bit more rigor.</p>

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<p>1 And even there, that's not 2 really peer review. All we're seeing is 3 what the person provided in the abstract. 4 We're not seeing the data. And I'm 5 telling you from looking at the data, 6 it's an extraordinary claim. 7 Q. If SGO accepts 25 percent of 8 abstracts for any type of presentation, 9 whether it be poster or meeting, do you 10 have any reason to doubt that figure? 11 MS. SHARKO: Well, I object 12 to the form of the question. 13 Lacks foundation. And I'm not 14 sure I understand it. 15 THE WITNESS: So -- 16 BY DR. THOMPSON: 17 Q. Did you understand the 18 question? 19 A. Not really. What's the 20 question? 21 DR. THOMPSON: Okay. You 22 can leave off the speaking 23 objections. 24 BY DR. THOMPSON:</p>	<p>1 retained? 2 A. No. 3 Q. Did Dr. Saed publish 4 articles regarding cancer biology prior 5 to 2017? 6 A. Yes. Apparently. I mean, 7 from his CV and from my backwards search 8 of his record. 9 Q. And did Dr. Saed publish 10 articles about inflammation and ovarian 11 cancer prior to 2017? 12 A. He published papers that 13 claim to be about inflammation, yes. 14 That's not the same thing. 15 Q. It's not the same -- 16 A. We'd have to go through each 17 paper. 18 Q. -- thing to claim and to be 19 about inflammation? 20 A. Well, we'd have to go 21 through the actual paper to see whether 22 it's convincing. 23 For example, he says he 24 publishes papers about oxidative stress,</p>
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<p>1 Q. The question is if SGO 2 represents that they accept 25 percent of 3 abstracts submitted at any level, do you 4 have any reason to dispute that? 5 A. I have no knowledge one way 6 or the other. I have no opinion on that 7 subject. 8 Q. Okay. And if SGO sends 9 abstracts to reviewers who identify 10 themselves as experts in the field, do 11 you have any reason to dispute that 12 representation? 13 A. I don't know what field 14 we're talking about. 15 Q. Molecular biology for 16 example? 17 MS. SHARKO: Object to the 18 form. Lacks foundation. 19 THE WITNESS: I have -- I 20 have no knowledge of what SGO 21 does. I don't go to SGO meetings. 22 BY DR. THOMPSON: 23 Q. Okay. Were you familiar 24 with Dr. Saed's work prior to being</p>	<p>1 but the papers just look at levels of 2 redox enzymes. And that alone does not 3 say anything about the net oxidative tone 4 in cells. You actually have to directly 5 measure it. 6 And as I said in my report, 7 he made these claims in his most recent 8 paper, which was just apparently 9 published, about oxidative stress. But 10 he never measured it. 11 So you can't really say that 12 there's a change in oxidative stress 13 without measurement. You actually have 14 to measure it. 15 He didn't measure 8-oxodG. 16 He didn't measure BODIPY. And he didn't 17 measure DCF florescence. Those are the 18 standard measurements, among others, for 19 looking at the net tone of reactive 20 oxygen species inside cells, or other 21 forms of reactive oxygen -- of -- of 22 oxidative stress like lipid peroxidation 23 or oxidative damage to DNA. 24 DR. THOMPSON: Object as</p>

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<p style="text-align: right;">Page 346</p> <p>1 nonresponsive. 2 BY DR. THOMPSON: 3 Q. Did he publish any articles 4 about ovarian cancer and oxidative stress 5 prior to 2017? 6 A. He did. And some of those 7 are among the most that are off -- the 8 most off point for this particular 9 question. 10 Q. Are you finished? 11 A. Mm-hmm. 12 Q. Did you review any of 13 Dr. Saed's pre-2017 articles? 14 A. Several of them, yes. 15 Q. And did you bring those with 16 you today? 17 A. As I told you at the 18 beginning of the deposition, I didn't 19 bring anything with me today except my 20 coat. 21 Q. Are they listed on your 22 materials considered list? 23 A. Anything that I read of 24 Dr. Saed's that I believe is relevant to</p>	<p style="text-align: right;">Page 348</p> <p>1 journals, including use of multiple 2 siRNAs and rescue controls. 3 So those -- those papers -- 4 which I'm absolutely sure I did cite 5 somewhere in this report, or at least I'm 6 pretty sure. We can go through my entire 7 report, but I'm pretty sure that I cited 8 those papers and that specific 9 information, that that gives me -- that 10 makes me question the quality of his 11 work. As I said in my report. 12 Q. But those papers were all 13 peer reviewed and published in journals, 14 correct? 15 A. As I said, none of his 16 papers are published in high -- in high 17 impact journals and the quality of review 18 at lower quality journals often matches 19 the quality of the journal. 20 Q. And you would consider 21 Gynecologic Oncology a lower tiered 22 journal? 23 A. I think it depends on what's 24 being published in Gynecological</p>
<p style="text-align: right;">Page 347</p> <p>1 this is referenced in thein the report. 2 Q. I did not see any articles 3 of Dr. Saed's listed. 4 A. Then I didn't think they 5 were relevant to the report. 6 Q. So you do not think any of 7 Dr. Saed's prior publications were 8 relevant to your opinion that Dr. Saed 9 lacks knowledge of basic cancer cell 10 biology, genetics and biochemistry? 11 A. No, I actually do think they 12 were. I think -- I'm pretty sure I cited 13 an earlier paper where he used -- where 14 he did -- where -- for example, where he 15 claimed that myeloperoxidase was in 16 cells. He did that based on immuno 17 staining, but he didn't have the proper 18 controls for myeloperoxidase. So all he 19 did was use an antibody. So that doesn't 20 prove that it's there. 21 And -- and his claims for 22 perturbation experiments involve the use 23 of siRNAs. And he didn't have the proper 24 controls that are required by all major</p>	<p style="text-align: right;">Page 349</p> <p>1 Oncology. There are very fine papers 2 published in Gynecological Oncology, but 3 it depends on the particular topic. 4 And high quality molecular 5 biology papers are rarely published in 6 Gynecologic Oncology. Some of them are. 7 Q. How about Cancer? 8 A. Cancer is a very low 9 quality -- a low impact journal. 10 Q. Would it be important for 11 you to -- to look at the methodology that 12 Dr. Saed had previously published in 13 papers? 14 A. As I just said, I did look 15 at the methodology. I always read papers 16 very extensively. When I -- I mean, one 17 of the things that I focus on most is the 18 methods. 19 I always teach my students 20 and postdocs that the methods are the 21 most important thing you can read when 22 evaluating a paper, because otherwise you 23 can't know whether the data are valid. 24 So, yes, I did extensively</p>

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<p>1 look at his work.</p> <p>2 Q. And you'll agree that</p> <p>3 Dr. Saed has considered the molecular</p> <p>4 changes in various histologic subtypes of</p> <p>5 ovarian cancer, right?</p> <p>6 A. What do you mean considered?</p> <p>7 Q. He's published use --</p> <p>8 using -- looking at molecular changes in</p> <p>9 histologic subtypes?</p> <p>10 A. I'm not sure which paper you</p> <p>11 are referring to, but I don't really</p> <p>12 think so.</p> <p>13 In fact, one of the features</p> <p>14 of Dr. Saed's work is he does not appear</p> <p>15 to be aware of the recent evidence from</p> <p>16 Domcke, et al. and others that</p> <p>17 traditional so-called ovarian cancer cell</p> <p>18 lines are not representative of ovarian</p> <p>19 cancer -- at least traditional serous</p> <p>20 ovarian cancer cell lines are not really</p> <p>21 serous cancer lines.</p> <p>22 So he uses standard ovarian</p> <p>23 cancer cell lines in some of his work</p> <p>24 subsequent to the publication of his work</p>	<p>1 a break.</p> <p>2 THE VIDEOGRAPHER: Remove</p> <p>3 your microphones, please. The</p> <p>4 time is 3:34 p.m. Off the record.</p> <p>5 (Short break.)</p> <p>6 THE VIDEOGRAPHER: We are</p> <p>7 back on the record. The time is</p> <p>8 3:58 p.m.</p> <p>9 BY DR. THOMPSON:</p> <p>10 Q. Dr. Neel, are all the</p> <p>11 criticisms that you have of Dr. Saed</p> <p>12 contained in your report?</p> <p>13 A. I believe so, yes.</p> <p>14 Q. Are there --</p> <p>15 A. Of the papers that are</p> <p>16 relevant to this case, yes.</p> <p>17 Q. And are all the papers that</p> <p>18 you relied upon for your criticisms with</p> <p>19 Dr. Saed contained in the report?</p> <p>20 A. I believe so, I'd have to --</p> <p>21 can I look through the references? I'm</p> <p>22 pretty sure, but -- I guess his new</p> <p>23 paper, I don't have the final citation</p> <p>24 for that. So that would not be in the</p>
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<p>1 such as Domcke, et al. in Nature</p> <p>2 Communications in 2013 that are not real</p> <p>3 serous cancer lines and yet he makes the</p> <p>4 claim that they are -- or he assumes that</p> <p>5 they are.</p> <p>6 So I did read those papers</p> <p>7 quite thoroughly. And I can tell you on</p> <p>8 multiple occasions his work is not</p> <p>9 scientifically conclusive and in some</p> <p>10 places categorically flawed.</p> <p>11 Q. Has Dr. Saed to your</p> <p>12 knowledge ever been reprimanded or</p> <p>13 sanctioned for publishing false data?</p> <p>14 A. I'm not accusing Dr. Saed of</p> <p>15 publishing false data. I'm accusing him</p> <p>16 of publishing bad science. I'm not</p> <p>17 accusing him of fraud. You only get</p> <p>18 reprimanded for fraud. Bad science, you</p> <p>19 just get a bad reputation.</p> <p>20 Q. Does Dr. Saed have a bad</p> <p>21 reputation?</p> <p>22 A. I don't know. But he does</p> <p>23 with me.</p> <p>24 DR. THOMPSON: Good time for</p>	<p>1 report.</p> <p>2 Let's see. I'd have to look</p> <p>3 through the report. If you want me to</p> <p>4 take the time, I'm happy to do it.</p> <p>5 Q. That's fine, because I need</p> <p>6 to know what literature you're relying on</p> <p>7 that forms the basis of your criticism of</p> <p>8 Dr. Saed.</p> <p>9 A. So I did read the paper. On</p> <p>10 Page 17, the statement that he made on</p> <p>11 his report on Page 5, ovarian cancer</p> <p>12 patients manifest significant -- because</p> <p>13 some of those refer to earlier papers,</p> <p>14 which I just read. But I just cited his</p> <p>15 statement in the report and pointed out</p> <p>16 that it wasn't really relevant to his</p> <p>17 contention for the purpose of this</p> <p>18 litigation. So I would have to go back</p> <p>19 and see what those papers were.</p> <p>20 Q. Where are you referring to?</p> <p>21 A. Page 17.A at the bottom.</p> <p>22 MS. SHARKO: We also served</p> <p>23 a supplemental materials</p> <p>24 considered list last night, DR.</p>

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<p>1 THOMPSON. I assume you have that. 2 DR. THOMPSON: Actually, I 3 intended to mark that. I don't -- 4 THE WITNESS: Yeah. The 5 same thing refers -- I'm sorry. I 6 didn't want -- the same thing 7 refers to Point B on Page 17. 8 That refers to an earlier paper by 9 Dr. Saed, which I just cited based 10 on his report. And his earlier 11 studies of -- the statements that 12 he made about the SNPs. So all of 13 those earlier papers on SNPs that 14 are not confirmed by the GWAS, 15 genomewide association studies to 16 be relevant to ovarian cancer, and 17 are listed here. 18 So I -- so I based it on his 19 report, and then I looked up the 20 actual SNPs to see whether what he 21 said had been confirmed by the 22 GWAS studies. 23 BY DR. THOMPSON: 24 Q. Is it your testimony that</p>	<p>1 not what we're discussing. We're 2 not discussing the produced 3 documents from Dr. Saed. 4 THE WITNESS: We can go 5 through his CV, and I'm happy to 6 point out which papers I read. 7 DR. THOMPSON: Okay. Let's 8 go ahead and do that. 9 THE WITNESS: So Number 1. 10 Number 2 is not relevant. 11 Number 3 is not relevant. 12 BY DR. THOMPSON: 13 Q. But, you'll agree that those 14 references are not included -- 15 A. I didn't read them. Like I 16 said -- 17 Q. Let me finish my question. 18 MS. SHARKO: Wait. She's 19 going to ask a new question. 20 BY DR. THOMPSON: 21 Q. That -- you'll agree that 22 those references were not included on 23 either your reference list or your 24 materials considered list, correct?</p>
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<p>1 you read every article that was included 2 in Dr. Saed's report? 3 A. I definitely looked at every 4 article that he authored that is in his 5 report. I can't remember if I read every 6 word. But I definitely looked at each of 7 them to see if I thought they were 8 directly relevant. And I probably read a 9 large fraction of them. 10 Q. And why are those not 11 included on your reference list? 12 A. Because I was referring to 13 them from his report. 14 MS. SHARKO: I mean, just so 15 there's no confusion. We gave Dr. 16 Neel all the exhibits and all the 17 documents that Dr. Saed produced 18 that's on Page 40. We didn't take 19 the time to list all that out. 20 MS. O'DELL: That's not what 21 he was referring to in terms -- he 22 wasn't referring to produced 23 documents. I think he was 24 referring to references. That's</p>	<p>1 A. Well, because for the 2 standpoint of my report, the fact that 3 it's not germane to the issue here is 4 what I was saying. 5 In other words, if you look 6 on Page 17, he makes this statement that 7 ovarian cancer patients manifest 8 significantly decreased levels of 9 antioxidants and higher level of 10 oxidants. 11 I say regardless of whether 12 the statement is true, it's a non 13 sequitur. That's why I didn't list it as 14 a reference. And I didn't consider those 15 papers as part of this report and part of 16 my opinion about, you know, the role of 17 talc and ovarian cancer because this is 18 not relevant. 19 So I looked at the paper. 20 Q. You're saying that statement 21 in A comes from one of his other papers? 22 A. He references the other 23 paper, but the issue is not relevant to 24 this case, because it has to do with</p>

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<p>1 what's happened in already developed 2 ovarian cancer. And the issue at hand is 3 whether talc produces oxidative stress 4 which causes ovarian cancer which occurs 5 before fully blown ovarian cancer. 6 So that's why I pointed out 7 it's not relevant. 8 Q. All right. So I'm entitled 9 to know every paper that you relied upon 10 for your opinions. 11 So if you need to go through 12 Dr. Saed's CV and you can tell me which 13 of these papers you read and relied upon, 14 let's go ahead and do that. 15 MS. SHARKO: I object to the 16 form of the question. There's a 17 difference between reading and 18 relied upon. Which do you want? 19 DR. THOMPSON: Okay. Well, 20 let's go with materials 21 considered, the title of his 22 reference list. 23 BY DR. THOMPSON: 24 Q. So --</p>	<p>1 DR. THOMPSON: That's -- 2 Dr. Neel -- 3 MS. SHARKO: I don't agree 4 with that. But anyway, go ahead. 5 BY DR. THOMPSON: 6 Q. Were all the -- were all the 7 publications that you reviewed of 8 Dr. Saed's included within the exhibits 9 from his deposition? 10 A. I'd have to look at his 11 deposition to be sure. 12 Q. Well, it was in your file, 13 right? 14 A. I know, but I don't have a 15 photographic memory of everything that 16 was in his deposition. 17 Q. And you didn't bring 18 anything with you here today? 19 A. I didn't bring anything with 20 me. 21 MS. SHARKO: Which is the 22 agreement of counsel. 23 MS. O'DELL: No, it's not. 24 We requested that materials that</p>
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<p>1 DR. THOMPSON: And none of 2 Saed's papers were on the 3 materials considered list, either 4 in the original or the 5 supplemental. So -- 6 MS. SHARKO: So I disagree 7 with you on that because the 8 exhibits to the depositions are, 9 the depositions are, his report 10 is, and his reported whatever it 11 was attached to it. 12 So I take issue with that. 13 That being said, if you want 14 to -- if you want to have Dr. Neel 15 go through the CV, the part of the 16 CV that's marked as Exhibit 29, 17 and tell you which ones he's read, 18 sure, you can do that. 19 MS. O'DELL: Exhibits to -- 20 exhibits to Dr. Saed's deposition 21 did not cover his previous 22 publications. So to suggest 23 otherwise, I think would be 24 incorrect.</p>	<p>1 were considered be brought to the 2 deposition. 3 There was no agreement that 4 those would not be brought here 5 today. You've asserted 6 objections, and some of which we 7 take issue with. But there's no 8 agreement that the materials would 9 not be brought. 10 MR. TISI: And I must tell 11 you, we have brought -- we have 12 brought every -- boxes of material 13 to every one of the depositions. 14 So this is another example 15 of you representing something that 16 really didn't happen. 17 So if you would tell us 18 where we agreed to that, I haven't 19 seen it. Because we've got boxes 20 and boxes and we gave it to you, 21 for example. 22 MS. SHARKO: There was no -- 23 Mr. Tisi, I'm not going to waste 24 your side's time having an</p>

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<p>1 argument.</p> <p>2 MR. TISI: Good, because you</p> <p>3 can't because there was no such</p> <p>4 agreement.</p> <p>5 You make these kinds of</p> <p>6 assertions repeatedly and they are</p> <p>7 just not true. So you --</p> <p>8 MS. SHARKO: You are totally</p> <p>9 wrong, Mr. Tisi.</p> <p>10 MR. TISI: So tell me where</p> <p>11 it is we agreed that he could not</p> <p>12 bring materials relied on, when we</p> <p>13 asked them in the notice of</p> <p>14 deposition.</p> <p>15 MS. SHARKO: We served</p> <p>16 objections to the deposition</p> <p>17 notice, which you have.</p> <p>18 MR. TISI: That's not an</p> <p>19 agreement.</p> <p>20 MS. SHARKO: There was no</p> <p>21 agreement to bring all the stuff</p> <p>22 that everybody reviewed. If</p> <p>23 there's something specific you</p> <p>24 want, let's figure it out and get</p>	<p>1 on.</p> <p>2 MR. TISI: Okay. Well, tell</p> <p>3 me where it is. Tell me where we</p> <p>4 agreed not to bring information</p> <p>5 relied on.</p> <p>6 MS. SHARKO: No.</p> <p>7 MR. TISI: Okay.</p> <p>8 MS. O'DELL: I think, tell</p> <p>9 us where and tell us who you</p> <p>10 believe made that agreement,</p> <p>11 because I can tell you the only</p> <p>12 other person that would have the</p> <p>13 authority to make that agreement</p> <p>14 is Michelle. She is not here. It</p> <p>15 would be Chris or myself.</p> <p>16 This is not true. So let's</p> <p>17 move on. But if you're going to</p> <p>18 take the position that you're not</p> <p>19 going to bring materials for</p> <p>20 experts in these depositions, then</p> <p>21 we need to take it up with Judge</p> <p>22 Pisano, because that's clearly not</p> <p>23 in compliance with the rules.</p> <p>24 MS. SHARKO: So -- so if</p>
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<p>1 it.</p> <p>2 MR. TISI: But he's -- but</p> <p>3 you said there was an agreement of</p> <p>4 counsel not to bring things, which</p> <p>5 is totally different than you</p> <p>6 objecting to something on the</p> <p>7 notice of deposition.</p> <p>8 MS. SHARKO: I disagree with</p> <p>9 you, Mr. Tisi.</p> <p>10 MR. TISI: Okay. Well, I</p> <p>11 think the record will --</p> <p>12 MS. SHARKO: You constantly</p> <p>13 make misrepresentations, Mr. Tisi,</p> <p>14 but that's --</p> <p>15 MR. TISI: That's a</p> <p>16 deflection. That's a deflection.</p> <p>17 You made an assertion,</p> <p>18 Susan, that there was an agreement</p> <p>19 of counsel not to bring</p> <p>20 information to the deposition that</p> <p>21 the witness relied on. That's not</p> <p>22 true. So --</p> <p>23 MS. SHARKO: I disagree -- I</p> <p>24 disagree with you. But let's move</p>	<p>1 there's -- there are things that</p> <p>2 you think should be brought to the</p> <p>3 depositions, let's talk about that</p> <p>4 afterwards.</p> <p>5 MR. TISI: Everything that</p> <p>6 was in the notice of deposition.</p> <p>7 Every -- because I -- you know,</p> <p>8 we -- we have depositions coming</p> <p>9 up and unless there's some basis</p> <p>10 like privilege or something like</p> <p>11 that, we expect you to bring them</p> <p>12 to the deposition.</p> <p>13 MS. SHARKO: All right. I'm</p> <p>14 not going to have this</p> <p>15 discussion --</p> <p>16 MR. TISI: Of course you</p> <p>17 don't want to.</p> <p>18 MS. SHARKO: -- now on the</p> <p>19 record.</p> <p>20 MR. TISI: Of course you</p> <p>21 don't want to. Because -- because</p> <p>22 we did it. We did it and you</p> <p>23 didn't.</p> <p>24 MS. SHARKO: Mr. Tisi, let's</p>

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<p>1 move on. 2 I'm happy to -- 3 MR. TISI: Okay. 4 MS. SHARKO: Leigh, I'm 5 happy to talk to you afterwards or 6 tomorrow. You'll probably be in 7 Atlantic City, right? 8 MS. O'DELL: We'll see. 9 MS. SHARKO: We'll see? 10 Okay. 11 The judge changed the time, 12 did you see that? 13 MS. O'DELL: I did see that. 14 BY DR. THOMPSON: 15 Q. Okay. 16 A. I looked through -- so I 17 want to clarify what I meant. 18 So I read several of these 19 papers to see if they were relevant and 20 I -- if I thought they were irrelevant, I 21 said they were irrelevant. 22 But if you want to know 23 which ones, it's what he cited in his 24 paper. But I -- I mean --</p>	<p>1 A. Yes, but several -- several 2 of them have, you know, statements which 3 are not true, like the thing about the 4 SNPs. 5 Q. Was the methodology that was 6 used in the previous publications and 7 peer reviewed relevant at all? 8 MS. SHARKO: Object to the 9 form of the question. 10 THE WITNESS: Yeah, I don't 11 know which particular methodology 12 or paper you're referring to. 13 BY DR. THOMPSON: 14 Q. Well, I'm saying if Dr. Saed 15 used the same or similar methods 16 publishing this paper that he did in 17 previous papers, is that relevant? 18 A. He didn't use the same 19 method. The -- the earlier work was just 20 based on small SNP analysis. This was 21 based on use of panels of SNPs, arrays of 22 SNPs. It's a -- it's a new -- relatively 23 -- it's a more modern method that's 24 available in the earlier papers.</p>
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<p>1 Q. Okay. Let's -- 2 A. -- there are very few 3 additional papers that are even cited by 4 him in his paper, in his report, that are 5 relevant. 6 Q. Okay. First off, let me 7 just ask you, are any of the papers 8 listed on Dr. Saed's CV relevant in your 9 mind? 10 A. The most relevant one is 11 the -- is the current one, which is the 12 one that was in press. And that's the 13 one that I criticized the most 14 specifically. 15 Many of the other ones are 16 cited by Dr. Saed as relevant, but they 17 aren't relevant in my opinion, as I state 18 in my report. 19 So, for example -- 20 Q. So -- okay. So no -- none 21 of Dr. Saed's previous publications that 22 are relevant in your opinion with the 23 exception of the one just published; is 24 that correct?</p>	<p>1 Q. But you'll agree with me 2 that there -- there's a lot of data in 3 Dr. Saed's paper that goes beyond just 4 the SNP analysis, correct? 5 A. The SNP analysis is the only 6 analysis which addresses the 7 extraordinary claim of a genotype switch 8 in response to talc treatment of cells. 9 So that is the only data. 10 What he should have done was 11 carry out Sanger sequencing, since he's 12 claiming that there is a wholesale change 13 in a genetic content of a specific 14 polynucleotide -- of a specific SNP 15 within 72 hours of talc treatment which 16 would be utterly unprecedented as far as 17 I know in molecular biology. 18 Q. Okay. Let's -- let's go 19 ahead and have you identify what articles 20 from Dr. Saed's CV that you considered. 21 A. Oh. For example, on Page 30 22 he said -- he had a paper, "Specific 23 point mutations and key redox enzymes are 24 associated with chemoresistance and</p>

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<p>1 epithelial ovarian cancer." I looked at 2 that paper and immediately concluded that 3 it was not relevant to this litigation or 4 the question of my report because it has 5 to do with fully blown ovarian cancer. 6 So I looked at the paper, 7 but it's not relevant for this, so I 8 didn't cite it in my reference. 9 Q. So which -- 10 A. Similarly -- 11 Q. -- which paper was that? 12 A. Reference 9. 13 Q. Give me a number -- 14 A. Page 30. 15 Q. Okay. So that one you 16 looked at and determined it was not 17 relevant? 18 A. Correct. 19 Q. Let's just go through, 20 and -- 21 A. Similarly -- 22 Q. -- tell me if there are 23 others -- 24 A. Reference 15 addresses a</p>	<p>1 how to answer that, because 2 there's obviously a legal issue 3 here that I don't understand. 4 But, I mean, if I read 5 something and it's not relevant to 6 my opinions, does that mean that I 7 considered it? Okay. Well, in 8 that case... 9 MS. SHARKO: That wouldn't 10 be my interpretation, but if 11 that's your question. That's 12 fine. 13 BY DR. THOMPSON: 14 Q. Well, it's fine to go ahead 15 and tell us whether or not you -- go 16 ahead and circle the ones that you read 17 and I may ask you questions. 18 A. Sure. Reference 26, I read. 19 It was relevant to something I'm 20 interested in, but it wasn't at all 21 germane. So I don't know how you would 22 count that one. 23 MS. SHARKO: By the way we 24 have the references in the</p>
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<p>1 similar subject. Not relevant. 2 Q. Oh, okay. 3 A. Reference -- I'm just 4 referring to -- 5 Q. Do you have the exhibit 6 there? 7 A. Yes. 8 Q. Would you go ahead and mark 9 on the exhibit? 10 A. I thought I'm not allowed to 11 mark the exhibits. 12 Q. You are if we ask you to. 13 A. Okay. Sure. 14 Q. Go ahead and -- just so 15 we'll have the record. Go ahead and mark 16 which ones that you considered. 17 MS. SHARKO: Considered 18 meaning read? 19 DR. THOMPSON: I'm just 20 using the language that's in the 21 statute, materials considered, and 22 what's on his reliance list -- on 23 his materials considered list. 24 THE WITNESS: I don't know</p>	<p>1 doctor's report in the other room 2 if you want them if you can't find 3 a paper. 4 DR. THOMPSON: Okay. 5 Thanks. 6 THE WITNESS: Again, 45 7 would fall under the same 8 category. That's it. Oh, wait 9 the review articles. 10 BY DR. THOMPSON: 11 Q. Dr. Neel, if you're 12 finished. 13 A. No, I didn't look at the 14 reviews. You can have your pen back too. 15 I am a pen stealer. I admit to that. 16 Q. So Dr. Neel, let me just ask 17 you about the articles that are circled 18 on Dr. Saed's CV, Exhibit 29, and have 19 you tell me whether these were papers 20 that you relied upon for your opinions or 21 decided were not relevant or any comments 22 that you want to make. 23 A. Sure. 24 MS. SHARKO: Except now he</p>

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<p>1 doesn't have a copy of it in front 2 of him. 3 DR. THOMPSON: That's true. 4 THE WITNESS: You can keep 5 handing it back and forth to me. 6 DR. THOMPSON: No, let me -- 7 or maybe share Ms. Sharko's copy. 8 MS. SHARKO: Okay. So my 9 copy won't have circles on it. 10 DR. THOMPSON: Right. I'll 11 tell you a number and you can tell 12 me. 13 That's probably even better. 14 BY DR. THOMPSON: 15 Q. On that exhibit, let's go 16 through the ones that are circled. If 17 you could just mark relevant or 18 irrelevant. "I" for irrelevant -- "I" 19 for irrelevant and "R" for relevant. How 20 is that? 21 MS. SHARKO: Those are the 22 only two choices? 23 BY DR. THOMPSON: 24 Q. If you have a different</p>	<p>1 my opinion that, you know, he's 2 misinterpreting the data. So I don't 3 know how to -- how to write that. 4 Q. And that paper was published 5 in Gynecologic Oncology, right? 6 A. Yes. 7 Q. And peer-reviewed, right? 8 A. Yes, as I said before, the 9 very fact that -- if it's not 10 peer-reviewed, it's completely unreliable 11 until it's peer-reviewed. But the fact 12 that it's been peer-reviewed doesn't make 13 it right. 14 Q. Do you know the -- 15 MS. SHARKO: Well, wait. 16 He's still going through the -- 17 through the last task. 18 THE WITNESS: I think 19 that's -- that's -- I think that's 20 all of them. Yeah. Okay. I 21 marked them all. 22 BY DR. THOMPSON: 23 Q. Okay. Thank you. Do you 24 recognize any of the other authors on</p>
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<p>1 choice, we can have a write-in candidate. 2 A. How about not directly 3 relevant, although it was cited by him as 4 relevant. 5 Ditto, not directly 6 relevant, although he asserted it was. 7 As I said, as I recall the 8 only one that's directly relevant is the 9 more recent one. And all the other ones 10 are claimed as being relevant but they're 11 off point, in my opinion. I'm going to 12 write the same thing on all the other 13 ones. There aren't that many, because 14 most of these papers are not directly 15 relevant. 16 So for example, Reference 52 17 is not -- this is the one where he, I 18 believe, shows -- I don't have the paper 19 in front of me. We'd have to look at it. 20 But I believe that's the paper where he 21 claims that myeloperoxidase expressed in 22 ovarian cancer cells. 23 So that's not relevant to 24 the topic at hand, but it is relevant to</p>	<p>1 these paper as you look through it? By 2 memory, name the authors that you 3 recognize. 4 A. I don't remember -- I mean, 5 I don't -- 6 Q. Could you just glance 7 through and see if you -- 8 A. Sure. 9 Q. -- recognize any of the 10 other authors. 11 A. Sure. 12 MS. SHARKO: On the ones 13 that he marked, right? 14 THE WITNESS: I recognize 15 Fletcher, because I know that 16 she's in the lab. I recognize her 17 name from the deposition. But I 18 don't know any of the other 19 authors. Fletcher again. 20 BY DR. THOMPSON: 21 Q. So is it fair to say, 22 Dr. Neel, that you don't know the 23 reputations of any of Dr. Saed's 24 co-authors on these papers?</p>

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<p>1 A. So far, that's fair to say, 2 yes. But I believe that the overwhelming 3 majority of them are people who are 4 working in his lab. 5 Q. Do you know that or are you 6 guessing? 7 A. No, I know that from the 8 papers that I remember reading, I think 9 most of them, it was from one lab. But I 10 could be -- we can go through each 11 individual paper if you want. But that 12 reputation -- reputation is not relevant 13 to me. 14 What's relevant to me is my 15 reading of the papers and assessment of 16 their scientific quality. And that's 17 what I did, and that's the basis for my 18 conclusions on Page 23, Point K. 19 Q. Let's switch gears a little 20 bit, Dr. Neel. 21 You looked at other papers 22 directly related to molecular effects of 23 talc or talcum powder as well, correct? 24 A. Most of which, we've already</p>	<p>1 Q. And you had actually quite a 2 few criticisms of this paper as well? 3 A. Yes. 4 Q. Correct? 5 A. Yes. Starting with the fact 6 that it's published in a journal that's 7 not really relevant to ovarian cancer or 8 cancer, Phytotherapy Research. I don't 9 think I've ever seen a paper on ovarian 10 cancer in Phytotherapy Research. 11 Q. But you'll agree that the 12 paper at least deals with ovarian cells 13 cultures and molecular effects, right? 14 A. A small part of the paper, 15 yeah. Yes. 16 Q. This paper was 17 peer-reviewed, right? 18 A. By somebody who reviews for 19 Phytotherapy Research, which is highly 20 unlikely to be anyone who is a credible 21 ovarian cancer researcher. 22 Q. And in the abstract of this 23 paper, the authors state, "Talc increased 24 proliferation, induced neoplastic</p>
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<p>1 discussed. But yes, everything that's in 2 my report is what I looked at. 3 Q. Let's talk about that 4 Buz'Zard paper that you read and included 5 in your report on Page 25. 6 A. Yes. Buz'Zard and Lau. 7 Q. I could have swore I put 8 those stickers right where I could find. 9 There they are. 10 DR. THOMPSON: This will be 11 Exhibit 30, the paper by Buz'Zard. 12 (Document marked for 13 identification as Exhibit 14 Neel-30.) 15 MS. SHARKO: Do we have a 16 29? 17 THE WITNESS: Maybe that was 18 the CV. 19 MS. SHARKO: Oh yeah. CV 20 was 29. I'm sorry. 21 BY DR. THOMPSON: 22 Q. Do you recall reading this 23 paper? 24 A. Absolutely.</p>	<p>1 transformation, and increased ROS 2 generation time dependently in the 3 ovarian cells and dose dependently in the 4 PNM." 5 Did I read that correctly? 6 A. Yes, you read the statement 7 correctly. 8 Q. And is it your opinion that 9 those statements do not actually reflect 10 what the experiments demonstrated? 11 A. Yes. It's my -- it's my 12 contention that this paper is highly 13 flawed in multiple ways, starting with -- 14 do you want me to tell you all the ways 15 that it's flawed? 16 Q. Sure. 17 A. Starting with the fact that 18 we have no idea what a -- if there -- if 19 talc does get from the perineum into the 20 fallopian tube or the ovarian surface 21 epithelial region, we have no idea of 22 what a relevant dose is. So picking 23 these doses has no biological relevance. 24 In fact, I don't think you</p>

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<p>1 can actually study the question unless 2 you have an idea of the dose of the agent 3 that gets to the relevant tissue. So the 4 first problem is the design of the 5 experiments is intrinsically flawed. 6 The second point -- 7 Q. Can we go one at a time -- 8 A. Sure. 9 Q. -- just because I have 10 question -- 11 A. Sure. Yeah, you asked me 12 to -- 13 Q. It will be easier -- yeah. 14 A. So that's my first problem. 15 Q. Aren't in vitro studies 16 frequently done for mechanistic purposes 17 and not necessarily to determine a 18 relevant dose? 19 A. It's well known that the 20 only relevant studies that are done in 21 vitro are done with a relevant dose of 22 the agent that you're testing. 23 So I can only comment on 24 well-designed and well-performed</p>	<p>1 powder that would be relevant? 2 A. I think it would be 3 impossible to do a compelling study until 4 you first answered the question of 5 whether perineum -- talc applied to the 6 perineum of a woman gets to the ovary and 7 at what dose -- 8 Q. How do you -- 9 A. The fallopian tube. 10 Q. How do you ascertain that 11 information? 12 A. It's not my -- I would have 13 to sit down and think it through. That's 14 not my purpose here today. 15 My purpose is not to do the 16 experiments for them. My purpose is to 17 evaluate the published data. 18 And my opinion is that the 19 study starts out being flawed by not 20 knowing anything about a relevant dose. 21 It's their obligation to figure out a 22 relevant dose, not mine. It's my 23 obligation to read their paper and decide 24 whether it's scientifically credible.</p>
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<p>1 experiments, not poorly designed and 2 poorly performed experiments. 3 Q. How would you know a 4 relevant dose if you wanted to look at 5 talcum powder in vitro and how it would 6 relate to women who are using talcum 7 powder regularly on their perineum? 8 A. That's exactly the point. 9 Q. So are the -- would all 10 molecular studies be worthless? 11 A. Until you can define a 12 reasonable dose, it doesn't -- you can't 13 do an experiment that's relevant to the 14 question at hand. 15 If you just go dumping talc 16 at various levels onto cells, it may have 17 absolutely no -- it probably has 18 absolutely no relevance to what happens 19 when you apply talc to the perineum of a 20 woman, and if and whether any degree of 21 talc gets to -- to the relevant tissue. 22 Q. So in your opinion, with our 23 current knowledge, it would be impossible 24 to do a molecular study with talcum</p>	<p>1 But that's the -- that's only the first 2 of many weaknesses of this study. 3 Q. We'll get -- we'll get to 4 some -- let me finish my question here 5 and then we'll get to the others. 6 Assuming that you did not 7 have a conflict of interest policy at 8 your institution, could you design a 9 study, a molecular study that you think 10 could be relevant to studying the issue 11 that we are talking about today? 12 A. I don't know. I haven't 13 really given it any thought. I haven't 14 given it significant thought. Maybe. 15 I'd have to think about it for a while. 16 Q. Okay. Let's go on with 17 your -- your criticisms. 18 Are these the same that are 19 outlined in your report? 20 A. Yes. 21 Q. Or are there additional 22 ones? 23 A. Yes, those are exactly the 24 criticisms. But I'm happy to go through</p>

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<p>1 each of them if you want.</p> <p>2 Q. Let's go ahead and go</p> <p>3 through them.</p> <p>4 A. Okay. Well, granular --</p> <p>5 most of the study, a large fraction of</p> <p>6 the study concerns granulosis cells which</p> <p>7 are not relevant to epithelial ovarian</p> <p>8 cancer of any type.</p> <p>9 Q. So is it your opinion that</p> <p>10 seeing biological effects on cells from</p> <p>11 anything other than tubal epithelium are</p> <p>12 irrelevant?</p> <p>13 A. Well, even if they had, you</p> <p>14 know, primary ovarian surface epithelium,</p> <p>15 that might be relevant because I think</p> <p>16 there is some evidence that some ovarian</p> <p>17 cancer come from the OSE, ovarian surface</p> <p>18 epithelial, OSE.</p> <p>19 But these cells are already</p> <p>20 transformed with SV40 large T antigen.</p> <p>21 And SV40 large T antigen inactivates the</p> <p>22 two major oncogenic pathways. It</p> <p>23 activates all members of the RV family</p> <p>24 and it inactivates p53. So these cells</p>	<p>1 It's well known that soft</p> <p>2 agar transformation in human cells is not</p> <p>3 predictive of -- of tumorigenicity which</p> <p>4 is the issue at hand.</p> <p>5 And the -- if you look</p> <p>6 carefully at the data, the -- the</p> <p>7 purported pro-oncogenic effects on</p> <p>8 cellular proliferation and on ROS occur</p> <p>9 at two different doses of talc.</p> <p>10 So notwithstanding my</p> <p>11 criticism about the dose in the first</p> <p>12 place, it's not known which of these</p> <p>13 doses would be relevant.</p> <p>14 So I think that pretty much</p> <p>15 covers it.</p> <p>16 Oh yeah, the</p> <p>17 polymorphonuclear leukocyte experiments</p> <p>18 are not relevant because, as we discussed</p> <p>19 earlier today, there is no evidence for</p> <p>20 white -- for poly -- or PMN infiltration</p> <p>21 into the premalignant lesions of -- of</p> <p>22 human fallopian lesions like STICs or</p> <p>23 stills or p53 signatures.</p> <p>24 So I don't really think</p>
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<p>1 are already transformed.</p> <p>2 So if you're trying to</p> <p>3 investigate the effects of a potential</p> <p>4 initiating event, then this study is</p> <p>5 irrelevant.</p> <p>6 Plus it's well known that</p> <p>7 SV40 large T transformed cells are</p> <p>8 genetically unstable and any -- and</p> <p>9 different lines are different. So it's</p> <p>10 really not generally accepted that you</p> <p>11 use a study where you transform cells</p> <p>12 with SV40 large T and -- and use that to</p> <p>13 infer something about normal biology.</p> <p>14 So I think that's a serious</p> <p>15 weakness of this study.</p> <p>16 Q. Okay. Next?</p> <p>17 A. The third point is that they</p> <p>18 don't show any tumor genicity studies.</p> <p>19 It would have been very easy for them to</p> <p>20 take these cells, treat them with talc</p> <p>21 and then inject them into</p> <p>22 immunoincompetent mice and at least see</p> <p>23 if there's any evidence of</p> <p>24 transformation.</p>	<p>1 there's much in this paper to support the</p> <p>2 case that talc is pro-oncogenic.</p> <p>3 Q. And --</p> <p>4 A. It's a very poor quality</p> <p>5 journal and it's -- I don't think these</p> <p>6 authors have ever published on this again</p> <p>7 as far as I can tell.</p> <p>8 Q. Is it -- is it fair to say</p> <p>9 your criticisms of the Buz'Zard paper are</p> <p>10 similar to those of Dr. Saed's paper?</p> <p>11 A. No. They're -- they are</p> <p>12 different.</p> <p>13 Q. In terms of being flawed?</p> <p>14 A. Well, I mean I would say</p> <p>15 that it's like Anna Karenina. They are</p> <p>16 flawed in different ways.</p> <p>17 Q. Fair enough. Let's --</p> <p>18 and -- and the -- the results and</p> <p>19 mechanism that the authors are proposing</p> <p>20 in this paper are -- are not even</p> <p>21 plausible in your mind?</p> <p>22 A. Plausibility requires good</p> <p>23 experiments. These are bad experiments.</p> <p>24 So based on this set of data, there is</p>

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<p style="text-align: right;">Page 390</p> <p>1 nothing that can be educed from this work 2 as to biological plausibility in my 3 opinion. 4 Q. Let's -- let's go next to 5 the Shukla paper. Do you remember -- 6 A. Shukla? 7 Q. -- seeing that paper? 8 A. I remember the paper -- I 9 remember the name. It's an unusual name 10 so I remember. But I don't recall the -- 11 I'd have to see the paper to actually 12 comment on it. 13 Q. I'll hand that to you now. 14 (Document marked for 15 identification as Exhibit 16 Neel-31.) 17 BY DR. THOMPSON: 18 Q. Did you review this paper, 19 Dr. Neel? 20 A. Yes. 21 Q. And I believe you discussed 22 this paper in your report as well, 23 correct? 24 A. I do. Can you tell me the</p>	<p style="text-align: right;">Page 392</p> <p>1 in the report. But let me just look at 2 it again. Oh, yeah. So again, this is 3 an SV40 Tag-immortalized 4 anchorage-dependent human ovarian 5 epithelial line, so it's -- 6 MS. SHARKO: You've got to 7 go much slower. Sorry. 8 THE WITNESS: Oh, I'm sorry. 9 On Page -- on Page 115 in the 10 left-hand column, midway through 11 under the methods, which I write 12 extensively, it's an -- the 13 authors use for ovarian surface 14 epithelial cells an SV40 15 Tag-immortalized, 16 anchorage-dependent human ovarian 17 epithelial cell line. 18 So this suffers from the 19 same issues that I just mentioned 20 for the Buz'Zard paper in that 21 it's using a cell line that 22 already has -- should I continue? 23 BY DR. THOMPSON: 24 Q. Yes, I'm sorry.</p>
<p style="text-align: right;">Page 391</p> <p>1 page though? 2 Q. Yes. 3 A. So I can make sure. 4 Q. It's Page 21. Beginning on 5 Page 21. 6 In this paper, the authors 7 reported -- 8 A. Hold on. I don't see it on 9 21. Can you tell me where it is on 21? 10 Q. Page 21 of your paper in the 11 last paragraph. 12 A. Oh, sure, yeah, yeah. 13 Sorry. It's in the middle. 14 Q. And in this paper the 15 authors report all -- alterations in gene 16 expression following exposure to asbestos 17 as well as talc in mesothelial and 18 ovarian surface cells, correct? 19 A. Yes. 20 Q. Do you have criticisms of 21 this paper? 22 A. Hold on. Let me go through 23 it again. It's been a while since I saw 24 it. And the criticisms that I have are</p>	<p style="text-align: right;">Page 393</p> <p>1 MS. SHARKO: Okay. 2 THE WITNESS: This paper 3 uses an SV40 Tag-immortalized 4 anchorage-dependent human ovarian 5 epithelial cell line which, 6 therefore, suffers from the same 7 issues that I raised earlier with 8 the paper by Buz'Zard and Lau in 9 that this -- these cell lines 10 are -- already suffered -- already 11 have had introduced a minimum of 12 two of the transforming events 13 that occur in ovarian cancer. 14 So the cell line is not 15 necessarily germane to the 16 initiating events of ovarian 17 cancer. That's the first thing. 18 The second thing is that the 19 paper primarily concerns, you 20 know, asbestos effects on 21 mesothelial cells, not so much the 22 effects of talc on ovarian 23 epithelial cells. 24 And if you look at the</p>

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<p>1 changes. In fact, if you go to 2 Page 2009. In contrast to 3 LP9/TERT and NYU474 mesothelial 4 cells, that's referring to the 5 pleural mesothelial cells. 6 IOSE cells showed no 7 significant gene upregulation or 8 downregulation in response to 9 lower concentrations of asbestos 10 and no significant mRNA changes 11 were observed with non-fibrous 12 talc, fine titanium dioxide, or 13 glass beads at either time point. 14 So the relevant cell type 15 shows no changes in gene 16 expression, and the irrelevant 17 cell type shows minimal changes in 18 gene expression in response to 19 talc. 20 So again, I don't really 21 think that Dr. Saed's quote is 22 relevant. So if you read my 23 report on Page 21, I refer to 24 Shukla, et al., in the context of</p>	<p>1 these cells -- 2 Q. Well, my question is -- 3 A. -- in terms of gene 4 expression. 5 Q. -- as to the relevance. 6 A. Well, it's not -- it's not 7 relevant, and it's not -- it doesn't 8 support the claim that ovarian cancer is 9 caused by talc. So in that way it's not 10 relevant. 11 Q. Would you consider this 12 paper reliable? 13 A. Reliable? I mean, they 14 measured -- insofar -- so it's reliable 15 in the sense that they've used 16 established techniques, and I'm sure that 17 the gene expression data is correct. 18 Reliable insofar as one can draw 19 conclusions about asbestos or talc, I 20 have no comment about what a relevant 21 dose would be of asbestos, because I 22 haven't researched that issue. But I do 23 have a comment, the same comment that I 24 raised earlier about a difficulty in</p>
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<p>1 Dr. Saed's citation, not -- not 2 because I think this is 3 necessarily germane. 4 I am responding to 5 Dr. Saed's claim it's germane and 6 showing that it isn't germane in 7 my opinion. 8 BY DR. THOMPSON: 9 Q. So your opinion -- 10 MS. SHARKO: He was reading 11 from 118, not 2009. 12 THE WITNESS: Oh, did I -- 13 DR. THOMPSON: I found it. 14 MS. SHARKO: You did. 15 THE WITNESS: I'm sorry. 16 MS. SHARKO: No problem. 17 THE WITNESS: Sorry. Thank 18 you. 19 BY DR. THOMPSON: 20 Q. And so this paper, in your 21 opinion, is not relevant for the issue 22 that we're discussing today? 23 A. Well, if anything, it says 24 there is almost no effect of talc on</p>	<p>1 knowing what would be a relevant dose of 2 talc. 3 But in this case, the doses 4 they chose had no significant effects. 5 So it's not germane unless the -- unless 6 the point is to say that talc doesn't 7 induce gene expression changes in the 8 human ovarian cells. 9 Q. If -- and is it your 10 understanding that this paper or these 11 authors used non fibrous talc in the 12 studies? 13 A. I don't recall. I have to 14 look at what they used. 15 Q. It's in the abstract or the 16 methods. 17 A. Well, I would prefer to use 18 the methods. 19 Q. Sure. 20 A. I have to look at it. I 21 have to go to the results because they 22 characterize the fibers. I'm not really 23 an expert in fibers. But I believe 24 Dr. Mossman is an expert for the</p>

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<p style="text-align: right;">Page 398</p> <p>1 defendant. So I think that she would 2 probably be better at explaining this 3 than I. 4 Yes, they claim that it's 5 non-fibrous talc. But again, I'm not an 6 expert in mineralogy or geology. So I 7 can't comment on the quality of their 8 evaluation. But I will say that it's 9 non-fibrous talc, according to the paper. 10 Q. And if Baby Powder were 11 shown to contain fibrous talc or 12 asbestos, how would that change your 13 opinions regarding the paper? 14 A. Well, it would just make 15 this paper even more irrelevant because 16 they didn't use Johnson & Johnson's 17 products. 18 Q. Do you know Dr. Mossman? 19 A. I don't know her. I know of 20 her reputation, but I don't know her. 21 Q. And you haven't spoken to 22 her -- 23 A. No. 24 Q. -- regarding this case?</p>	<p style="text-align: right;">Page 400</p> <p>1 familiar, Dr. Neel? 2 A. Yes. 3 Q. And did you read this paper? 4 A. A while ago, yes. 5 Q. Do you -- 6 A. I don't remember if I 7 actually -- was there a place in my 8 report that you want to discuss here? 9 Q. I don't believe that -- oh, 10 actually, I think you did discuss this in 11 here. Let me find it. Yes, it's on Page 12 24. 13 A. 24. I thought I remember 14 typing that. Yes. 15 Q. And do you have criticisms 16 regarding this paper? 17 A. Yes. As outlined in my 18 report on Page 24. 19 Q. And what are those? 20 A. These authors measured the 21 effects of talc on A549 cells, which are 22 lung cancer cells, and found ROS 23 production, oxidation of cellular lipids, 24 and DNA damage.</p>
<p style="text-align: right;">Page 399</p> <p>1 A. I've never met her or spoken 2 to her. 3 Q. I believe you had two papers 4 by Dr. Akhtar on your materials 5 considered list. Does that sound 6 familiar? 7 A. Yeah. I don't know if 8 that's the -- I didn't know how to 9 pronounce that name. 10 Q. I don't either so you're -- 11 does anyone? 12 A. It sounds like it's right. 13 A-H-K or something? 14 MS. SHARKO: That's 15 Exhibit 32. 16 (Document marked for 17 identification as Exhibit 18 Neel-32.) 19 DR. THOMPSON: 32 is the 20 Akhtar paper. 21 BY DR. THOMPSON: 22 Q. "The Primary Role of Iron 23 Mediated Lipid Peroxidation." 24 Does this paper look</p>	<p style="text-align: right;">Page 401</p> <p>1 So, again, these are already 2 established lung cancer cells. So I 3 don't see the relevance to the question 4 of initiation of ovarian cancer. That's 5 first thing. 6 The second thing is that -- 7 the same issues having to do with dose 8 are germane here. And I guess I should 9 see -- I don't remember which form of 10 talc they used. Yeah, so commercial 11 talc. So again, those are my main 12 criticisms. 13 They use dose -- again, as I 14 said, it's not clear as the dosage used 15 here or seen here relate to the small 16 number of particles that are presumably 17 found in the reproductive tract, if 18 they're there at all. 19 Q. Are you aware that Dr. Saed 20 used the same dosage as Dr. Akhtar 21 reported in his paper? 22 A. I'd have to look to be sure. 23 But perhaps. Dr. Saed's papers are 24 seriously flawed, as we've already</p>

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<p style="text-align: right;">Page 402</p> <p>1 discussed.</p> <p>2 Q. Yeah, I understand your</p> <p>3 opinion as to that. The author's first</p> <p>4 sentence in the abstract is, "Talc</p> <p>5 particles, the basic ingredient in</p> <p>6 different kinds of talc-based cosmetic</p> <p>7 and pharmaceutical products, pose a</p> <p>8 health risk to pulmonary and ovarian</p> <p>9 systems due to domestic and occupational</p> <p>10 exposures."</p> <p>11 Do you disagree with that</p> <p>12 statement --</p> <p>13 A. Yes.</p> <p>14 Q. -- that Dr. Akhtar makes?</p> <p>15 A. Yes.</p> <p>16 Q. Do you think that Akhtar</p> <p>17 is -- Dr. Akhtar is not credible?</p> <p>18 A. I have no knowledge as to</p> <p>19 Dr. Akhtar. I have never met him. Don't</p> <p>20 know anything about him. Don't know his</p> <p>21 reputation and can't comment on it.</p> <p>22 Q. This paper was peer reviewed</p> <p>23 and published?</p> <p>24 A. Yes. And I also can't</p>	<p style="text-align: right;">Page 404</p> <p>1 glutathione depletion."</p> <p>2 Those were at least some of</p> <p>3 the same things that Dr. Saed studied,</p> <p>4 correct?</p> <p>5 A. No, actually -- no, that's</p> <p>6 not correct. Actually, the major</p> <p>7 weakness of Dr. Saed's paper is he did</p> <p>8 not measure. As I said earlier, if you</p> <p>9 are going to claim a difference in redox</p> <p>10 balance, you have to measure redox</p> <p>11 balance by measuring ROS generation in</p> <p>12 the form DCF fluorescence or other types</p> <p>13 of ROS sensor assays. Lipid peroxidation</p> <p>14 by BODIPY staining or other methods like</p> <p>15 -- oxidative damage to DNA by ADG</p> <p>16 staining, none of which Dr. Saed did, as</p> <p>17 I said earlier.</p> <p>18 Q. Did you -- do you have any</p> <p>19 other criticisms of this paper?</p> <p>20 A. My -- my major point about</p> <p>21 this paper as I've said already, is that</p> <p>22 it concerns already developed lung cancer</p> <p>23 cells and it is well known in the</p> <p>24 scientific literature that there is</p>
<p style="text-align: right;">Page 403</p> <p>1 comment, since I'm not a toxicologist, on</p> <p>2 the quality of this journal. But I think</p> <p>3 it's probably not a high impact journal</p> <p>4 or a high quality journal.</p> <p>5 Q. Do you know if nanoparticles</p> <p>6 would apply to Johnson's Baby Powder?</p> <p>7 A. As I said, I am not -- not a</p> <p>8 mineralogist, I'm not a toxicologist. I</p> <p>9 can't comment on any of that.</p> <p>10 Q. So you --</p> <p>11 A. I don't have any</p> <p>12 professional opinion on that.</p> <p>13 Q. So you really have no idea</p> <p>14 as to the particle size of Johnson's Baby</p> <p>15 Powder?</p> <p>16 A. I have no idea as to the</p> <p>17 particle size.</p> <p>18 Q. And the authors a little</p> <p>19 further down in the abstract state, "Both</p> <p>20 varieties of talc nanoparticles</p> <p>21 differentially induce lipid peroxidation</p> <p>22 which was correlated with the pattern of</p> <p>23 lactate dehydrogenase leakage, reactive</p> <p>24 oxygen species generation, and</p>	<p style="text-align: right;">Page 405</p> <p>1 differences between the effects of ROS in</p> <p>2 cancer cells that are already</p> <p>3 established, and in particular, in cancer</p> <p>4 cell lines that have been passive for</p> <p>5 many years, and in particular, in</p> <p>6 different types of cancer cells than are</p> <p>7 present in normal cells.</p> <p>8 So the paper is -- is not</p> <p>9 germane in my opinion to the question of</p> <p>10 whether talc causes ROS changes and</p> <p>11 reactive oxygen induced damage in primary</p> <p>12 fallopian tube epithelium or primary</p> <p>13 ovarian surface epithelium.</p> <p>14 That is the relevant</p> <p>15 question. Notwithstanding all the issues</p> <p>16 about dose that we've talked about.</p> <p>17 Q. You'll agree though that the</p> <p>18 authors of this paper at least thought</p> <p>19 that their experiment was relevant for</p> <p>20 ovarian cancer, right?</p> <p>21 A. I have no idea --</p> <p>22 MR. LOCKE: Objection.</p> <p>23 BY DR. THOMPSON:</p> <p>24 Q. Well, they stated it that,</p>

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<p style="text-align: right;">Page 406</p> <p>1 in the first sentence, that --</p> <p>2 A. They -- they said that --</p> <p>3 Q. -- it poses a risk to</p> <p>4 pulmonary and ovarian systems.</p> <p>5 A. Well, that's their opinion.</p> <p>6 That doesn't say whether they thought</p> <p>7 they were -- whether they thought it was</p> <p>8 relevant. All they can say is that it --</p> <p>9 that assuming that everything in this</p> <p>10 paper is correct, in terms of the</p> <p>11 measurements and all that, which I have</p> <p>12 no reason to question, they can't say</p> <p>13 anything about dose, and they can't say</p> <p>14 anything about the relevant cells.</p> <p>15 So, cells are not cells.</p> <p>16 It's not like, you know, parts is parts</p> <p>17 in Perdue chicken.</p> <p>18 Q. What's you -- what's your</p> <p>19 basis for opinion that the -- the cells</p> <p>20 used in this experiment are not relevant</p> <p>21 for ovarian surface epithelium?</p> <p>22 A. Well, as I've already said,</p> <p>23 they are lung cancer cells. They -- they</p> <p>24 are a mutation. So A-549 cells have KRAS</p>	<p style="text-align: right;">Page 408</p> <p>1 providing, that lung cancer cells are</p> <p>2 irrelevant to the ovary in terms of study</p> <p>3 of this issue?</p> <p>4 MS. SHARKO: Object to the</p> <p>5 form of the question.</p> <p>6 THE WITNESS: Can you repeat</p> <p>7 the question? I'm not sure, there</p> <p>8 was a lot of --</p> <p>9 BY DR. THOMPSON:</p> <p>10 Q. Yeah, it was a bad -- it was</p> <p>11 a bad -- it was a bad question.</p> <p>12 A. Sorry.</p> <p>13 Q. Can you point me to an</p> <p>14 article that's on your reference list or</p> <p>15 materials considered list that addresses</p> <p>16 the basis for your opinion that lung</p> <p>17 cancer cells are irrelevant to ovarian</p> <p>18 cancer?</p> <p>19 A. I -- I didn't say lung</p> <p>20 cancer cells were irrelevant to ovarian</p> <p>21 cancer, although I would agree largely</p> <p>22 with that statement.</p> <p>23 What I said was lung cancer</p> <p>24 cells -- the use of lung cancer cells to</p>
<p style="text-align: right;">Page 407</p> <p>1 mutations. I believe it's -- it's either</p> <p>2 G12B or G12D, and that is completely</p> <p>3 irrelevant to the overwhelming majority</p> <p>4 of serous cancers, much less serous</p> <p>5 ovarian cancer transformation.</p> <p>6 So it's a lung epithelial</p> <p>7 cell. It's a transformed lung epithelial</p> <p>8 cell. It's bearing a mutation that is</p> <p>9 not found characteristically in serous</p> <p>10 cancer, and it's bearing a mutation that</p> <p>11 when it's found in serous cancer is not</p> <p>12 part of the initiating events in serous</p> <p>13 cancer.</p> <p>14 So irrelevant cell type,</p> <p>15 irrelevant mutations, irrelevant stage of</p> <p>16 carcinogenesis, and questionable dose.</p> <p>17 I -- I don't really see anything that</p> <p>18 could possibly be relevant to the</p> <p>19 question at hand when every other issue</p> <p>20 is irrelevant.</p> <p>21 Q. Is there any publication on</p> <p>22 your reference list or your materials</p> <p>23 considered list that would provide</p> <p>24 insight into that opinion that you're</p>	<p style="text-align: right;">Page 409</p> <p>1 determine the effects of agents on</p> <p>2 nontransformed ovarian epithelial cells</p> <p>3 or fallopian tube epithelial cells is</p> <p>4 irrelevant.</p> <p>5 And I think that should be</p> <p>6 self-evident to any practicing scientist</p> <p>7 in the cancer biology field. I don't</p> <p>8 think you would find any scientist,</p> <p>9 credible cancer biologist, who would</p> <p>10 think that using A-549 cells to model any</p> <p>11 aspect of ovarian cancer pathogenesis is</p> <p>12 relevant.</p> <p>13 Q. Well --</p> <p>14 A. And I would reject</p> <p>15 categorically from the six journals that</p> <p>16 I'm an editor of any paper that presumed</p> <p>17 to do the same, which is probably why a</p> <p>18 journal -- a paper like this is published</p> <p>19 in a low impact, low quality journal, and</p> <p>20 not in any of the six journals that I'm</p> <p>21 an editorial board member of or that I've</p> <p>22 been an editor of previously.</p> <p>23 Q. I understand that. But we</p> <p>24 have to be able to explain your opinions</p>

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<p style="text-align: right;">Page 410</p> <p>1 to nonscientists. And it would be --</p> <p>2 will be helpful to be able to refer to an</p> <p>3 article or something that can address the</p> <p>4 irrelevance of -- of using these cell</p> <p>5 lines to study ovarian cancer</p> <p>6 pathogenesis.</p> <p>7 And my question is, is there</p> <p>8 a citation on your reference or materials</p> <p>9 cited -- materials considered list that</p> <p>10 we could refer to to help?</p> <p>11 MS. SHARKO: Object. Object</p> <p>12 to the form.</p> <p>13 THE WITNESS: I don't think</p> <p>14 I would have any trouble</p> <p>15 convincing anybody who is logical</p> <p>16 that studying a fully transformed</p> <p>17 lung cancer cell is not relevant</p> <p>18 to studying a normal fallopian</p> <p>19 tube cell.</p> <p>20 I think that stems from</p> <p>21 elemental logic and you don't</p> <p>22 really even have to have much</p> <p>23 scientific credentials to make</p> <p>24 that conclusion.</p>	<p style="text-align: right;">Page 412</p> <p>1 personal -- first of all, I heard</p> <p>2 that. And it's not a personal</p> <p>3 opinion.</p> <p>4 That is a scientific opinion</p> <p>5 based on 39 years of research, and</p> <p>6 I don't think you will ever find a</p> <p>7 credible scientific expert in the</p> <p>8 field of cancer biology who would</p> <p>9 say that studying A-549 in cancer</p> <p>10 cells from the lung is relevant to</p> <p>11 understanding the pathogenesis of</p> <p>12 fallopian tube and/or ovarian</p> <p>13 cancer. It's simply irrelevant.</p> <p>14 And, again, I can cite and</p> <p>15 did cite in my report the fact</p> <p>16 that high grade serous cancer is</p> <p>17 not categorized by KRAS mutations.</p> <p>18 These cells have KRAS mutations.</p> <p>19 Okay? I know that because we work</p> <p>20 with these cells in a different</p> <p>21 context.</p> <p>22 BY DR. THOMPSON:</p> <p>23 Q. So if there were a scientist</p> <p>24 that would give an opinion that there is</p>
<p style="text-align: right;">Page 411</p> <p>1 BY DR. THOMPSON:</p> <p>2 Q. So that opinion at least is</p> <p>3 based on logic, not peer-reviewed medical</p> <p>4 literature; is that correct?</p> <p>5 A. That -- that --</p> <p>6 MS. SHARKO: Object to the</p> <p>7 form. Misstates the testimony.</p> <p>8 THE WITNESS: That opinion</p> <p>9 is based on 39 years of experience</p> <p>10 in the cancer biology field from</p> <p>11 its earliest days. And from the</p> <p>12 general understanding of cell</p> <p>13 biology, molecular biology, and</p> <p>14 cancer biology that I and many</p> <p>15 other scientists of my credibility</p> <p>16 and credentials would hold.</p> <p>17 BY DR. THOMPSON:</p> <p>18 Q. As far as referring me to a</p> <p>19 citation in your report or attachments,</p> <p>20 that would address this issue, you are</p> <p>21 not able to do that today?</p> <p>22 MS. SHARKO: Objection.</p> <p>23 Asked and answered several times.</p> <p>24 THE WITNESS: That's not a</p>	<p style="text-align: right;">Page 413</p> <p>1 relevance to studying the effects of</p> <p>2 talcum powder or some other potential</p> <p>3 carcinogen on cell lines other than</p> <p>4 normal tubal primary cell lines, would</p> <p>5 you automatically have a criticism of</p> <p>6 that particular scientist?</p> <p>7 A. I would have to see the</p> <p>8 scientist's opinion in detail, but</p> <p>9 anybody who -- anybody with training in</p> <p>10 modern cancer biology and with an</p> <p>11 understanding that A-549 cells are lung</p> <p>12 epithelial, the adenocarcinoma cells that</p> <p>13 bear a KRAS mutation, and anyone who knew</p> <p>14 about the pathogenesis of high grade</p> <p>15 serous ovarian cancer would realize that</p> <p>16 that's not a relevant cell system.</p> <p>17 I would expect a first year</p> <p>18 graduate student to know that, frankly,</p> <p>19 and even a good undergraduate.</p> <p>20 Q. There are certain carcinogen</p> <p>21 that cause cancer in many different</p> <p>22 tissues and different types of cancer,</p> <p>23 aren't there?</p> <p>24 A. There are some carcinogens</p>

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<p style="text-align: right;">Page 414</p> <p>1 that have the capacity to damage DNA in 2 many types of tissues, yes. 3 Q. And an example would be 4 asbestos, would it not? 5 A. As I said, I haven't really 6 exhaustively looked at the literature for 7 asbestos and cancer. But the only, you 8 know, thing that I know for sure is that 9 asbestos causes mesothelioma and is a 10 cocarcinogen with tobacco smoke for lung 11 cancer. 12 Q. So you are not aware of 13 other organs in which asbestos has been 14 shown to cause cancer as well? 15 A. I just said it's a cause of 16 mesothelioma. And it's a cocarcinogen 17 with tobacco smoke for lung epithelial 18 cancer. And there's some evidence it may 19 also cause lung epithelial cancer. 20 Q. And you have the IARC 2012 21 monograph on asbestos. Can you identify 22 the other types of cancer that IARC 23 concluded were caused by asbestos in 24 addition to mesothelioma?</p>	<p style="text-align: right;">Page 416</p> <p>1 developed cancer cells. 2 The question at hand, as I 3 understand the question, is does talc 4 contribute to the cause of ovarian 5 cancer. Once you have a fully -- fully 6 transformed lung cancer cell, it's a 7 cancer. 8 Q. But we have discussed 9 earlier that at least part of the 10 carcinogenic process includes promotion 11 and -- and progression of the cancer, 12 correct? 13 A. This cancer is a fully 14 developed, fully formed cancer. It's 15 gone way behind the progression and 16 initiation stages. This cancer will kill 17 a mouse if you inject it into a mouse. 18 It's not -- it's not a precancerous 19 lesion. It's not a cancer -- it's not a 20 lesion that it is in the process of 21 carcinogenesis. It's fully blown lung 22 cancer cell line derived probably from a 23 metastatic lung cancer patient who 24 underwent surgery. So it -- it's really</p>
<p style="text-align: right;">Page 415</p> <p>1 A. I -- 2 MS. SHARKO: Object to the 3 form. 4 THE WITNESS: I said that I 5 haven't really studied the IARC 6 monograph, so I can't comment on 7 that. 8 BY DR. THOMPSON: 9 Q. And would anyone who relies 10 on studies looking at the cell lines that 11 you've been discussing, that you deem 12 irrelevant, would they be wrong for doing 13 so? 14 A. I didn't say that the cell 15 lines were irrelevant. I said the cell 16 lines were irrelevant to the question at 17 hand. 18 These cell lines are highly 19 relevant to understanding lung cancer 20 pathogenesis. But they are not relevant 21 to understanding ovarian cancer 22 pathogenesis. 23 Q. Okay. Sir -- 24 A. And these cells are fully</p>	<p style="text-align: right;">Page 417</p> <p>1 not relevant in my opinion. 2 Q. Okay. 3 (Document marked for 4 identification as Exhibit 5 Neel-33.) 6 BY DR. THOMPSON: 7 Q. I'm going to give you 8 another paper by the -- at least Akhtar 9 is the same. 10 This is Exhibit 33, Akhtar, 11 "Cytotoxicity and apoptosis induction by 12 nanoscale talc particles." 13 Have you seen this paper, 14 Dr. Neel? 15 A. 70 and 71, that must be -- 16 Q. Oh, that's the -- 17 A. Let me see if that's the 18 paper that I cited. It's -- 19 MS. SHARKO: Yes. 20 THE WITNESS: Yeah, I've 21 seen this paper. I refer to it in 22 my report. It's in the context of 23 the same issues that we just 24 discussed.</p>

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<p style="text-align: right;">Page 418</p> <p>1 BY DR. THOMPSON: 2 Q. And are your criticisms of 3 this paper similar to the other Akhtar 4 paper? 5 A. Yes, it -- yes, again uses a 6 single lung cancer cell line which is 7 fully transformed and bears KRAS 8 mutations and, therefore, is not relevant 9 to nontransformed fallopian tube 10 epithelium or ovarian surface epithelium. 11 Nor is it relevant to serous cancer 12 pathogenesis because serous cancers 13 almost never have KRAS mutations, and 14 when they do have KRAS mutation, they are 15 a later stage of development and are not 16 involved in the initial stages of cancer. 17 That is well established 18 from modern molecular biology research. 19 Q. And this paper was peer 20 reviewed and published, correct? 21 A. I assume so. What journal 22 is this? I don't even know what 23 journal -- I assume it was. 24 Q. And the authors at least</p>	<p style="text-align: right;">Page 420</p> <p>1 of this paper are pretty much the same as 2 the criticisms I have with the other 3 Akhtar paper. Irrelevant cell line, 4 uncertain dose. You know, no 5 demonstration. We -- they couldn't 6 actually demonstrate carcinogenesis here 7 because they start with a cancer. 8 Q. Would you say that all four 9 of these molecular studies relating to 10 talc are flawed in some way? 11 A. I only count two. 12 MS. SHARKO: Object. Object 13 to the form. 14 THE WITNESS: We're only 15 discussing two. 16 BY DR. THOMPSON: 17 Q. Oh, I'm including Buz'Zard 18 and Shukla. 19 A. Oh yes, they are all 20 completely flawed from the standpoint of 21 the question at hand, yes. They are not 22 even close to being on point in my 23 opinion, professional opinion, based on 24 39 years of research in cancer biology</p>
<p style="text-align: right;">Page 419</p> <p>1 concluded that the particles that they 2 used which were commercial -- indigenous 3 and commercial nano talc particles, 4 right? 5 A. That is what they say, yes. 6 Q. Okay. And the authors at 7 least conclude that the particles 8 significantly induced cytotoxicity, 9 oxidative stress and apoptosis in human 10 lung epithelial cells? 11 A. Well, first of all, they are 12 not human lung epithelial cells. As I 13 said that's a misstatement. They are 14 human lung cancer cells. 15 So the title is misleading. 16 And that conclusion is misleading. 17 Human lung epithelial cells 18 can -- would normally be interpreted as, 19 say, normal human lung epithelial cells. 20 So these are human lung cancer cells. 21 That would be a more accurate statement. 22 Q. Do you have other criticisms 23 of the -- this paper? 24 A. The criticisms that I have</p>	<p style="text-align: right;">Page 421</p> <p>1 dating from the -- from the earliest days 2 of the field and staying current in 3 modern molecular biology research. 4 DR. THOMPSON: Would this be 5 a good time for a break? 6 MS. SHARKO: Again? 7 DR. THOMPSON: How long has 8 it been? 9 MS. O'DELL: A little over 10 an hour. I think it's an 11 appropriate time for a break. 12 THE VIDEOGRAPHER: Remove 13 your microphones. The time is 14 5:03 p.m. Off the record. 15 (Short break.) 16 THE VIDEOGRAPHER: Okay. We 17 are back on the record. The time 18 is 5:24 p.m. 19 BY DR. THOMPSON: 20 Q. Dr. Neel, we've looked at 21 five molecular studies this afternoon. 22 That paper by Saed, by Shukla, Buz'Zard, 23 and two by Akhtar. 24 Is it your opinion that all</p>

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<p>1 five of those studies are flawed? 2 A. They are either flawed or 3 they are not relevant. 4 Q. And the -- the reason for 5 that criticism seems to be primarily that 6 there is no established dose and that the 7 wrong cell lines are used. Is that a 8 fair statement? 9 A. That is -- 10 MS. SHARKO: Object to the 11 form. 12 THE WITNESS: That statement 13 refers to some of the papers. But 14 Dr. Saed's paper is flawed on 15 multiple levels, most notably his 16 claim that talc applied to ovarian 17 cells or fallopian tube cells can 18 produce a stoichiometric shift in 19 nucleotide sequence for a specific 20 gene. That is just an incredible 21 assertion. 22 So -- and also his claims 23 that redox balance is disrupted in 24 the cells without any measurement</p>	<p>1 BY DR. THOMPSON: 2 Q. Sure. 3 A. She distracted me. Sorry. 4 Q. So -- 5 MS. SHARKO: Sorry, that was 6 not my intention. 7 BY DR. THOMPSON: 8 Q. So is it your opinion that 9 any scientist who relied on those studies 10 to formulate their opinions as to whether 11 talcum powder use could cause ovarian 12 cancer, would be using poor judgment from 13 a scientific standpoint? 14 A. Yes. I would have to say 15 that. 16 Q. And would it be your opinion 17 that any scientist who relied on those 18 studies to answer the question of whether 19 talcum powder use could cause ovarian 20 cancer, would not have a sufficient 21 understanding of molecular and cellular 22 biology? 23 A. If that's the basis for 24 their opinion, then they are not -- yes,</p>
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<p>1 of redox balance in the cells. 2 You can't make that claim without 3 actually measuring redox balance. 4 So his paper, the -- the one 5 that's in -- that just was 6 published apparently is flawed 7 conceptually and technically. 8 The other papers are using 9 questionable doses and irrelevant 10 cell systems. So they're 11 different objections to the 12 different studies. 13 BY DR. THOMPSON: 14 Q. So is it your opinion that 15 any scientist who relies on these studies 16 would be using -- relying on these 17 studies to answer the question of whether 18 talcum powder causes ovarian cancer, 19 would be using bad scientific judgment? 20 MS. SHARKO: Object to the 21 form of the question. 22 THE WITNESS: What -- what 23 would -- can you repeat the 24 question?</p>	<p>1 that would be my opinion. 2 Q. Would -- would you look at 3 your CV which is exhibit -- something not 4 very high. 5 A. Yes. I have it. 6 Q. Okay. And before we get to 7 your CV, was -- would it be your opinion 8 that any scientist who relies on these 9 studies for opinions on the biological 10 plausibility of talcum powder use causing 11 ovarian cancer to be using poor 12 scientific judgment? 13 MS. SHARKO: I object to the 14 form of the question. Can you 15 break it down by study? 16 MS. O'DELL: No. 17 THE WITNESS: So if the -- 18 if the only studies that they used 19 to reach the opinion that talc 20 caused ovarian cancer were these 21 five highly flawed studies, they 22 would be exercising poor 23 scientific judgment in my opinion. 24 BY DR. THOMPSON:</p>

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<p style="text-align: right;">Page 426</p> <p>1 Q. Even on biological 2 plausibility? 3 A. Oh, for sure, yes. I don't 4 think these -- these papers are credible 5 assessments of biologic plausibility at 6 all in any way. 7 Q. And if the scientists who 8 rely on these studies for their opinions 9 regarding the biological plausibility of 10 talcum powder use causing ovarian cancer 11 would also not have a sufficient 12 understanding of molecular cellular 13 biology? 14 MS. SHARKO: Object to the 15 form of the question. 16 THE WITNESS: I -- I think 17 that it would depend on what -- 18 they might have an understanding 19 of some aspects of cell and 20 molecular biology. But they would 21 not have any understanding of 22 other aspects of cellular and 23 molecular biology. So that's a 24 very difficult question to answer.</p>	<p style="text-align: right;">Page 428</p> <p>1 products can cause ovarian cancer? 2 A. No. As I've said before, I 3 haven't studied that issue and I wouldn't 4 be able to study that issue in my current 5 position. 6 Q. Okay. Have you ever 7 published in Gynecologic Oncology, to 8 your knowledge? 9 A. I may have been a co-author 10 on a paper in Gynecologic Oncology. But 11 I have not been a senior author on any 12 paper in Gynecologic Oncology. 13 Q. Should any study that treats 14 ovarian cancer as a single entity be used 15 with skepticism? 16 A. I think today, yes. 17 Q. Is this because ovarian 18 cancer is not a single disease? 19 A. Yes. 20 Q. But isn't hormone -- hormone 21 responsiveness a common link among all 22 ovarian cancer subtypes? 23 A. Hormone responsive -- the 24 endometrioid and clear cell cases are</p>
<p style="text-align: right;">Page 427</p> <p>1 If you ask a more specific 2 question, I can help you with an 3 answer. 4 BY DR. THOMPSON: 5 Q. But at least the opinions 6 relating to the biological plausibility 7 for that, to answer that question, their 8 understanding in your opinion would be 9 inadequate? 10 A. I think that someone who 11 read these papers and thought that they 12 provided plausibility for the contention 13 that talc causes ovarian cancer would 14 have poor scientific judgment as to that 15 question, yes. 16 Q. Let's go ahead and look at 17 your CV now. 18 A. Sure. 19 Q. And we'll do the same thing 20 we did before. So using your criteria of 21 an established dose, an appropriate cell 22 line, are there any of your publications 23 that you think are relevant to the 24 question as to whether talcum powder</p>	<p style="text-align: right;">Page 429</p> <p>1 much more clearer about hormone 2 responsiveness. Whether serous cancers 3 are hormone responsive probably -- it 4 depends on the cancer. 5 So -- and whether it's 6 involved in pathogenesis is also not as 7 well established. 8 Q. But at least some scientists 9 would argue that hormone responsiveness 10 would be one of those factors that could 11 cross all histologic subtypes? 12 A. Again, I can't comment on 13 specific -- on general statements like 14 some scientists. If you give me a 15 specific statement that was made by a 16 specific scientist, I can look at it and 17 I can determine whether I agree with it 18 or not or whether I think it's credible. 19 Q. Has it been published that 20 hormone responsiveness would be a factor 21 that would cross all subtypes to your 22 knowledge? 23 A. There have been -- there -- 24 there have been reports that hormone</p>

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<p style="text-align: right;">Page 430</p> <p>1 replacement therapy may be oncogenic, you 2 know, procarcinogenic in ovarian cancer. 3 Q. And that includes all 4 subtypes? 5 A. Well, the effects are much 6 stronger for, as I said clear cell and 7 endometrial cancers. And whether it's 8 true for high grade serous is less clear, 9 from my -- from my recollection of the 10 literature. 11 Q. Could a reasonable scientist 12 discuss ovarian breast cancer and 13 endometriosis as a group because they are 14 all hormonally responsive lesions? 15 MS. SHARKO: Object to the 16 form of the question. 17 THE WITNESS: Discuss in 18 what context? I don't understand 19 the question. 20 MS. SHARKO: You can ask 21 them to read their handwriting. 22 BY DR. THOMPSON: 23 Q. If you were looking at in 24 vitro studies, would it be appropriate to</p>	<p style="text-align: right;">Page 432</p> <p>1 Q. Has that been studied? 2 A. I don't know the answer to 3 that question, so I would be 4 uncomfortable answering it. 5 Q. Could a reasonable scientist 6 make that statement? 7 A. I don't know. I'd have to 8 see the paper. I'm happy to look at the 9 paper and go over the data if there is 10 such a paper. 11 Q. Could inflammation-induced 12 proliferation in the tubal epithelium, in 13 the epithelial, if that did occur, 14 progress to papillary tubal hyperplasia? 15 A. What do you mean by 16 papillary tubal hyperplasia? Do you mean 17 STICs? 18 Q. Let's say STICs. 19 A. I don't know. I'd have 20 to -- I'd have to see the study. I'm not 21 going to speculate on mechanisms that I 22 haven't seen in the -- in the press -- in 23 the scientific press. 24 Q. In addition to the Saed</p>
<p style="text-align: right;">Page 431</p> <p>1 use either serous breast or endometrioid 2 cancer cell lines and extrapolate the 3 information from one to the other? 4 A. What's the question? Not 5 what's your question, but what's the 6 scientific question that's being asked? 7 I mean, if you want to just look at 8 hormone responsive gene expression, then 9 maybe. If the question is having to do 10 with the pathogenesis of each of the 11 individual diseases, then probably not. 12 It would depend on the 13 specifics though. Scientists don't think 14 that way. They think in very specific 15 terms so they can frame accurate 16 questions that can yield results that are 17 interpretable. So I can't answer a 18 question that's so generic and 19 nonspecific as that. 20 Q. Can chronic inflammation 21 induce a proliferation of tubal 22 epithelium? 23 A. I don't know the answer to 24 that question.</p>	<p style="text-align: right;">Page 433</p> <p>1 papers that you did not list in the 2 materials considered or the supplemental 3 materials, are there any other papers 4 that were -- that form the basis of your 5 criticisms of either the Saed or the 6 other molecular papers? 7 MS. SHARKO: Object to the 8 form of the question. Lacks 9 foundation. 10 THE WITNESS: I think you 11 misunderstood or maybe I was 12 unclear before. 13 My opinion of the Saed paper 14 that was just published is based 15 on the Saed paper that was just 16 published. 17 And that doesn't need me to 18 read any of his earlier papers. 19 My comments about some of 20 his earlier papers had -- went to 21 the issue of erroneous statements 22 that were made in his report. 23 Having to do, for example, with 24 the expression of myeloperoxidase</p>

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<p style="text-align: right;">Page 434</p> <p>1 and ovarian cancer cells, having 2 to do with the statement that p53 3 is an oncogene, whereas it's a 4 paradigmatic tumor suppressor 5 gene, having to do with statements 6 regarding SNPs that are not in the 7 GWAS catalogue of well-recognized 8 ovarian cancer SNPs. 9 But that had nothing to do 10 with my criticisms of his paper, 11 which stand independent of any 12 other issues regarding Dr. Saed's 13 qualifications or expertise. 14 DR. THOMPSON: Object as 15 nonresponsive. 16 BY DR. THOMPSON: 17 Q. Because my question was 18 really only, are there any other papers 19 or literature that form the basis? 20 A. With respect, DR. THOMPSON, 21 the question that you asked me, as I 22 understand it, and you're welcome to read 23 it back to me, but I believe your 24 question was, were there any other papers</p>	<p style="text-align: right;">Page 436</p> <p>1 clarify, were there -- the papers that 2 you considered informing those opinions 3 regarding Dr. Saed that you have not 4 mentioned so far? 5 A. No. 6 Q. Okay. Have you sent any 7 comments to Health Canada? 8 A. No. 9 Q. Do you plan to send any 10 comments to Health Canada? 11 A. I don't know if it's 12 appropriate for me to send any comments 13 to Health Canada while I'm involved in 14 this litigation. I would have to consult 15 Ms. Sharko and Mr. Zellers as to whether 16 I should. 17 Q. You'll agree that talc and 18 its potential contribution to ovarian 19 cancer has been an issue for several 20 decades. Would you agree with that, in 21 the literature? 22 A. It's certainly been in the 23 epidemiological literature. In the 24 biology literature, there's actually</p>
<p style="text-align: right;">Page 435</p> <p>1 that led to my objection to his, you 2 know, paper in Reproductive Biology. 3 And the answer to that is 4 none of those other papers are directly 5 relevant to the paper in Reproductive 6 Biology. The errors in the paper of 7 Reproductive Biology stand on their own 8 and are clearly determinable by anyone 9 with expertise in modern cellular and 10 molecular biology. 11 MS. SHARKO: Okay. I think 12 it's late. I think she's just 13 asking you if there are any papers 14 that you're relying on that aren't 15 listed in the report and reliance 16 materials. 17 THE WITNESS: No. 18 BY DR. THOMPSON: 19 Q. And Ms. Sharko is correct. 20 That was the question that I was trying 21 to ask. 22 A. Okay. And that question is 23 no. 24 Q. And I'm just going to</p>	<p style="text-align: right;">Page 437</p> <p>1 relatively limited studies, which is why 2 we've been actually able to cover most of 3 them in this last hour or two. 4 Q. And that would be for talc, 5 but certainly there have been studies 6 regarding the molecular basis for 7 asbestos and it's carcinogenic potential, 8 correct? 9 A. As I said, I haven't done an 10 exhaustive study of what's in the 11 literature about asbestos and its role in 12 ovarian cancer. I think you asked me 13 about talc, which is what I answered. 14 Q. I asked you about talcum 15 powder. Or I meant to ask about talcum 16 powder. 17 A. Yes. And I answered that. 18 Q. Have you ever been asked to 19 do an in vitro study with talcum powder? 20 A. No. 21 Q. Have you ever been asked to 22 do an in vivo study with talcum powder? 23 A. No. 24 Q. And could you do either an</p>

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<p style="text-align: right;">Page 438</p> <p>1 in vitro study or an in vivo study to 2 evaluate the causal connection between 3 talcum powder or the potential causal 4 connection between talcum powder and 5 ovarian cancer? 6 A. Not in my -- 7 MS. SHARKO: Objection. 8 Asked and answered a zillion 9 times. 10 THE WITNESS: I'll -- 11 that's -- 12 BY DR. THOMPSON: 13 Q. This question -- sorry. 14 This question is outside the context of 15 your current situation. 16 Could you do that study? 17 A. Could I do the study? I 18 would have to really seriously think 19 about the problem and then decide whether 20 I could do a good study. There would be 21 several problems, many of which I've 22 already described, having to do with 23 coming to arrive at a reasonable dose. I 24 probably could test a range of doses in a</p>	<p style="text-align: right;">Page 440</p> <p>1 and more physiologically relevant 2 systems than, for example, 3 Dr. Saed did, and certainly the 4 other four papers which were off 5 point in my opinion. 6 DR. THOMPSON: I have no 7 further questions. 8 MS. SHARKO: Okay. We're 9 done. Thank you very much. 10 THE WITNESS: Thank you. 11 THE VIDEOGRAPHER: Okay. 12 Stand by, please. This marks the 13 end of today's deposition. The 14 time is 5:42 p.m. 15 (Excused.) 16 (Deposition concluded at 17 approximately 5:42 p.m.) 18 19 20 21 22 23 24</p>
<p style="text-align: right;">Page 439</p> <p>1 biologically relevant system than, for 2 example, any of the five papers that we 3 discussed extensively in the last two 4 hours did. 5 Q. So at least today, sitting 6 here, you're not sure whether you could 7 do the quality study that would be 8 required or not; is that fair? 9 MS. SHARKO: Object to the 10 form. 11 THE WITNESS: I'm saying 12 that it's not clear that enough 13 information is available to design 14 a study, not that I couldn't do 15 it. I could certainly do it if a 16 reasonable -- if there were clear 17 information about a dose range of 18 talc that was in -- if there were 19 talc in fallopian tube and/or 20 there were talc in ovarian 21 adnexa -- in the adnexa -- in the 22 ovarian surface endothelium or 23 region, I could do a reasonable 24 study using those doses of talc</p>	<p style="text-align: right;">Page 441</p> <p>1 2 CERTIFICATE 3 4 5 I HEREBY CERTIFY that the 6 witness was duly sworn by me and that the 7 deposition is a true record of the 8 testimony given by the witness. 9 10 It was requested before 11 completion of the deposition that the 12 witness, BENJAMIN G. NEEL, M.D., Ph.D., 13 have the opportunity to read and sign the 14 deposition transcript. 15 16 MICHELLE L. GRAY, 17 A Registered Professional 18 Reporter, Certified Shorthand 19 Reporter, Certified Realtime 20 Reporter and Notary Public 21 Dated: March 20, 2019 22 23 (The foregoing certification 24 of this transcript does not apply to any reproduction of the same by any means, unless under the direct control and/or supervision of the certifying reporter.)</p>

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<p>1 INSTRUCTIONS TO WITNESS</p> <p>2</p> <p>3 Please read your deposition</p> <p>4 over carefully and make any necessary</p> <p>5 corrections. You should state the reason</p> <p>6 in the appropriate space on the errata</p> <p>7 sheet for any corrections that are made.</p> <p>8 After doing so, please sign</p> <p>9 the errata sheet and date it.</p> <p>10 You are signing same subject</p> <p>11 to the changes you have noted on the</p> <p>12 errata sheet, which will be attached to</p> <p>13 your deposition.</p> <p>14 It is imperative that you</p> <p>15 return the original errata sheet to the</p> <p>16 deposing attorney within thirty (30) days</p> <p>17 of receipt of the deposition transcript</p> <p>18 by you. If you fail to do so, the</p> <p>19 deposition transcript may be deemed to be</p> <p>20 accurate and may be used in court.</p> <p>21</p> <p>22</p> <p>23</p> <p>24</p>	<p>1</p> <p>2 ACKNOWLEDGMENT OF DEPONENT</p> <p>3</p> <p>4 I, _____, do</p> <p>5 hereby certify that I have read the</p> <p>6 foregoing pages, 1 - 445, and that the</p> <p>7 same is a correct transcription of the</p> <p>8 answers given by me to the questions</p> <p>9 therein propounded, except for the</p> <p>10 corrections or changes in form or</p> <p>11 substance, if any, noted in the attached</p> <p>12 Errata Sheet.</p> <p>13</p> <p>14</p> <p>15</p> <p>16 BENJAMIN G. NEEL, M.D., Ph.D. DATE _____</p> <p>17</p> <p>18</p> <p>19 Subscribed and sworn</p> <p>20 to before me this _____</p> <p>21 _____ day of _____, 20 ____.</p> <p>22 My commission expires: _____</p> <p>23</p> <p>24 Notary Public</p>
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Exhibit B

Ie-Ming Shih, M.D., Ph.D.

Page 1

IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF NEW JERSEY

- - -

IN RE: JOHNSON & :
JOHNSON TALCUM POWDER :
PRODUCTS MARKETING, :
SALES PRACTICES, AND : NO. 16-2738
PRODUCTS LIABILITY : (FLW) (LHG)
LITIGATION :
:
THIS DOCUMENT RELATES :
TO ALL CASES :

- - -

March 26, 2019

- - -

Videotaped deposition of
IE-MING SHIH, M.D., Ph.D., taken pursuant
to notice, was held at Venable, LLP, 750
East Pratt Street, Baltimore, Maryland,
beginning at 9:06 a.m., on the above
date, before Michelle L. Gray, a
Registered Professional Reporter,
Certified Shorthand Reporter, Certified
Realtime Reporter, and Notary Public.

- - -

GOLKOW LITIGATION SERVICES
877.370.3377 ph | 917.591.5672 fax
deps@golkow.com

Ie-Ming Shih, M.D., Ph.D.

Page 2	Page 4
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Page 3	Page 5
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2 (Pages 2 to 5)

Ie-Ming Shih, M.D., Ph.D.

Page 6				Page 8			
1	---			1	---		
2	E X H I B I T S (Cont'd.)			2	DEPOSITION SUPPORT INDEX		
3	---			3	---		
4				4			
5	NO. DESCRIPTION PAGE			5	Direction to Witness Not to Answer		
6	Shih-10 Pre-Diagnostic 275			6	PAGE LINE		
7	Serum Levels of				None.		
8	Inflammation Markers			7			
9	(Trabert)			8	Request for Production of Documents		
10	Shih-12 Papillary Tubal 411			9	PAGE LINE		
11	Hyperplasia: The				None.		
12	Putative Precursor			10			
13	(Kurman)			11	Stipulations		
14	Shih-15 The Hallmarks of 305			12	PAGE LINE		
15	Cancer				None.		
16	(Hanahan)			13			
17	Shih-16 Hallmarks of 308			14	Questions Marked		
18	Cancer: The			15	PAGE LINE		
19	Next Generation				333 10		
20	Shih-20 Journal of 361			16			
21	Ovarian Research			17			
22	Role of CA-125			18			
23	(Gupta)			19			
24	Shih-21 Tumor-Associated 365			20			
	Autoantibodies as			21			
	Early Detection			22			
	(Kaaks)			23			
	Shih-22 Early Detection 370			24			
	Of Ovarian Cancer						
	(Elias)						
Page 7				Page 9			
1	---			1	THE VIDEOGRAPHER: We are		
2	E X H I B I T S (Cont'd.)			2	now on the record.		
3	---			3	My name is Daniel Holmstock.		
4				4	I'm the videographer for Golkow		
5	NO. DESCRIPTION PAGE			5	Litigation Services.		
6	Shih-23 Identifying Post 378			6	Today's date is March 26,		
7	Menopausal Women			7	2019.		
8	At Elevated			8	The time on the video screen		
9	Risk for Epithelial			9	is 9:06 a.m.		
10	Ovarian Cancer			10	This video deposition is		
11	(Urban)			11	being held at the Law Offices of		
12	Shih-24 Critical Questions 384			12	Venable LLP, at 750 East Pratt		
13	In Ovarian Cancer			13	Street, Suite 900 in Baltimore,		
14	Research and			14	Maryland, In Re Johnson & Johnson		
15	Treatment			15	Talcum Powder Products Marketing,		
16	(Bast)			16	Sales Practices, and Products		
17	Shih-26 Smoking and 432			17	Liability Litigation, MDL number		
18	Carcinoma of the Lung			18	2738, pending before the United		
19	(Doll, Hill)			19	States District Court for the		
20	Shih-27 Methylomic Analysis 102			20	Eastern District of New Jersey.		
21	Of Ovarian Cancers			21	Our deponent today is		
22	(Pisanic)			22	Dr. Ie-Ming Shih.		
23	Shih-29 Reported Incidence 125			23	Counsel for appearances will		
24	And Survival of			24	be noted on the stenographic		
	Fallopian Tube						
	Carcinomas						
	(Trabert)						
	Shih-30 Genomics of 136						
	Ovarian Cancer						
	Progression(Eckert)						
	Shih-39 Molecular Basis 213						
	Supporting the						
	Association of						
	Talcum Powder Use						
	(Fletcher)						

3 (Pages 6 to 9)

Ie-Ming Shih, M.D., Ph.D.

Page 10	Page 12
<p>1 record.</p> <p>2 Our court reporter is</p> <p>3 Michelle Gray, who will now</p> <p>4 administer the oath.</p> <p>5 - - -</p> <p>6 ... IE-MING SHIH, M.D., Ph.D.,</p> <p>7 having been first duly sworn, was</p> <p>8 examined and testified as follows:</p> <p>9 - - -</p> <p>10 EXAMINATION</p> <p>11 - - -</p> <p>12 BY DR. RESTAINO:</p> <p>13 Q. Good morning, Dr. Shih.</p> <p>14 A. Good morning.</p> <p>15 Q. My name is John Restaino,</p> <p>16 and I will be the attorney asking you</p> <p>17 some questions today. I note from the</p> <p>18 materials we have received that you have</p> <p>19 been deposed before, correct?</p> <p>20 A. Correct.</p> <p>21 Q. But I still -- there's still</p> <p>22 a few things that I want to go over</p> <p>23 because I heard you talk about water</p> <p>24 before the deposition started. We will</p>	<p>1 Q. And I will too. And so far</p> <p>2 we've been doing fine. But there's the</p> <p>3 court reporter to your right and my left,</p> <p>4 and she's going to try to take down</p> <p>5 everything we say. And if we -- all of</p> <p>6 us were having a normal conversation on a</p> <p>7 Friday evening somewhere, it's not</p> <p>8 uncommon to step on each others'</p> <p>9 sentences without being rude.</p> <p>10 But today, if we do that,</p> <p>11 then in essence we are being rude to the</p> <p>12 court reporter. So I will do my best to</p> <p>13 listen for that final period in your</p> <p>14 answer, if you will do your best to</p> <p>15 listen for the question mark on mine.</p> <p>16 Agreed?</p> <p>17 A. Okay.</p> <p>18 Q. Now, I'm going to hand you</p> <p>19 what was previously marked this morning</p> <p>20 as Plaintiffs' Exhibit Number 1, which is</p> <p>21 the notice of the deposition.</p> <p>22 MR. ROTMAN: I handed you</p> <p>23 one earlier, right?</p> <p>24 DR. RESTAINO: Yes, I gave</p>
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<p>1 be taking a break about every hour or so;</p> <p>2 however, in between that period of time,</p> <p>3 if you need to take a break for whatever</p> <p>4 reason, you just let us know. Do you</p> <p>5 understand?</p> <p>6 A. Yes.</p> <p>7 Q. Today is not going to be a</p> <p>8 memory test for you. So if you need to</p> <p>9 review documents, it's open book.</p> <p>10 And if you -- and it's not a</p> <p>11 physical test. So once again, feel free</p> <p>12 to call for a break whenever you need to</p> <p>13 if we don't. Do you understand that?</p> <p>14 A. Okay.</p> <p>15 Q. Now, it's important that you</p> <p>16 let me know if you don't understand my</p> <p>17 question. If I become tongue-tied or I</p> <p>18 use different terminology that you're not</p> <p>19 used to, let me know and I'll repeat the</p> <p>20 question. But if you answer a question,</p> <p>21 the presumption will be that you</p> <p>22 understood the question. Agreed?</p> <p>23 A. I will try my best to answer</p> <p>24 your question.</p>	<p>1 it back to Michelle.</p> <p>2 MR. ROTMAN: These are the</p> <p>3 other copies.</p> <p>4 (Document marked for</p> <p>5 identification as Exhibit</p> <p>6 Shih-1.)</p> <p>7 BY DR. RESTAINO:</p> <p>8 Q. Doctor, have you seen that</p> <p>9 before?</p> <p>10 A. I remember I saw it --</p> <p>11 Q. Okay.</p> <p>12 A. -- recently.</p> <p>13 Q. If you would turn to Page 4,</p> <p>14 it becomes the language that's most</p> <p>15 germane to this morning. You see Number</p> <p>16 1, we're requesting your most current</p> <p>17 curriculum vitae.</p> <p>18 Have you provided that to</p> <p>19 us?</p> <p>20 A. I believe so.</p> <p>21 Q. Thank you.</p> <p>22 Number 2 is copies of any</p> <p>23 materials that pertain to your retention</p> <p>24 or payment for services as an expert.</p>

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<p style="text-align: right;">Page 14</p> <p>1 And have you provided, for example, any 2 retainer agreement that you may have? 3 A. I don't remember I have a 4 retention agreement. 5 Q. Okay. Have you provided any 6 documents, invoices, for the time that 7 you have incurred so far in the 8 litigation since you've been retained as 9 an expert? 10 A. I sent J&J attorney my 11 invoice. 12 Q. This morning I was provided 13 with an invoice for the draft of expert 14 opinion report dated January 19, 2019. 15 And it states from December 12th to 16 Jan -- of 2018 to January 19th of 2019. 17 And this invoice is for a 18 total of 18 hours at \$800 an hour and 19 \$14,400. Does that sound familiar -- 20 MS. MILLER: Can we have a 21 copy of that? 22 THE WITNESS: Can I see it? 23 Can I see the document? 24 BY DR. RESTAINO:</p>	<p style="text-align: right;">Page 16</p> <p>1 since January 19, 2019, on this matter? 2 A. I do not have an exact 3 number, because this is still ongoing, 4 and I'm very busy. But I would give you 5 my estimation. About 90 hours, 6 plus/minus 15 hours. 7 Q. Okay. Have you provided to 8 counsel and through counsel to us any 9 records that you may have in the sense of 10 notes, draft materials, anything that 11 comprise your folder, for example, on the 12 study you have conducted? 13 MS. MILLER: Wait. 14 Objection. If you're talking 15 about draft materials related to 16 his report, that would be 17 privileged, as you know. Are you 18 asking for draft materials related 19 to his report, or are you only 20 asking about his -- what you're 21 calling his study? 22 DR. RESTAINO: His study. 23 MS. MILLER: Okay. Can you 24 explain what you mean by his</p>
<p style="text-align: right;">Page 15</p> <p>1 Q. Yes. 2 A. And can I review it? 3 MS. MILLER: Dr. Shih, it's 4 redacted because the work you did 5 is confidential, so we blacked 6 this out. 7 THE WITNESS: Okay. 8 Understand. 9 MS. MILLER: This is not the 10 way it looked when you sent it to 11 us. 12 BY DR. RESTAINO: 13 Q. Does that look familiar, 14 sir? 15 A. Yes. 16 Q. Does that look accurate? 17 A. Correct. 18 Q. And may I assume that you 19 have put in more hours since January 19th 20 of 2019? 21 A. I spent additional times on 22 this matter. 23 Q. Okay. Can you estimate for 24 us how much more time you have spent</p>	<p style="text-align: right;">Page 17</p> <p>1 study. 2 BY DR. RESTAINO: 3 Q. You have attached to your 4 expert report in the back a document that 5 is a study of analysis that you've 6 conducted of histopathology slides, 7 correct? 8 A. Could you show me where you 9 are talking about? 10 Q. Sure. Why don't we go 11 ahead, and I'm going to hand you what we 12 have marked as Exhibit Number 2. 13 (Document marked for 14 identification as Exhibit 15 Shih-2.) 16 BY DR. RESTAINO: 17 Q. And this is your expert 18 report. This obviously, you're going to 19 want to keep open and next to you. 20 MR. ROTMAN: John, give me 21 one, please. 22 (Document marked for 23 identification as Exhibit 24 Shih-3.)</p>

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<p style="text-align: right;">Page 18</p> <p>1 BY DR. RESTAINO: 2 Q. I'm going to hand you what 3 we have marked as Exhibit Number 3. This 4 is titled "Curriculum Vitae Version 5 February 8, 2019." 6 (Document marked for 7 identification as Exhibit 8 Shih-4.) 9 BY DR. RESTAINO: 10 Q. Exhibit 4 is a document 11 titled "Study Report to Determine Whether 12 Chronic Inflammation Causes Ovarian 13 Cancer." 14 MS. MILLER: This isn't 15 numbered. Do you have one with a 16 sticker? 17 DR. RESTAINO: Sorry. That 18 one was for you. 19 THE WITNESS: I would like 20 to make sure these are my copies. 21 BY DR. RESTAINO: 22 Q. Okay. What do you mean by 23 making sure that it's your copy? 24 A. There is no missing pages</p>	<p style="text-align: right;">Page 20</p> <p>1 publication Number 123 is, could you tell 2 me without looking? 3 MS. MILLER: Objection. 4 THE WITNESS: I know my 5 right quote, but I cannot remember 6 every word and sequence, if you 7 want to test my memory. 8 BY DR. RESTAINO: 9 Q. No, sir. I don't want to 10 test your memory, but you just spent a 11 lot of time going through your CV -- CV 12 to see if anything was missing. 13 How would you know if 14 anything was missing from your CV if you 15 don't have it memorized? 16 A. I look at the pages to see 17 whether they are in sequence, or anything 18 unusual that I don't put it in my 19 original CV. 20 Q. Okay. So the pages are 21 numbered like, for example, 1 through 53, 22 correct? 23 A. 1 to 53. 24 Q. Is that correct?</p>
<p style="text-align: right;">Page 19</p> <p>1 and additional material. 2 Q. You are now looking at 3 your -- the exhibit that's your study 4 report, sir? 5 A. I want to make sure there's 6 no missing pages or additional material 7 inserted. 8 Q. Sir, are you finished? 9 A. I guess so. 10 Q. Okay. Sir, do you have your 11 curriculum vitae which we've marked as 12 Exhibit 3 and you have gone through, do 13 you have that document memorized? 14 A. Could you repeat your 15 question one more time? 16 Q. Your -- your CV that you 17 just went through, do you have that 18 document memorized in your mind? 19 MS. MILLER: Objection. 20 THE WITNESS: What do you 21 mean memorize? 22 BY DR. RESTAINO: 23 Q. Do you know it by heart? If 24 I was to ask you to write down what</p>	<p style="text-align: right;">Page 21</p> <p>1 A. Yes. 2 Q. So in order to determine 3 whether or not there were any pages 4 missing, all you had to do was look at 5 the page numbers at the bottom, instead 6 of running your finger down every 7 publication, isn't that true? 8 A. I want to make sure -- 9 MS. MILLER: Objection. 10 Please give me time to 11 object. These questions are 12 objectionable. 13 THE WITNESS: Okay. Sure. 14 BY DR. RESTAINO: 15 Q. Now, you also looked at the 16 document which I believe we've marked as 17 Number 4, which is your study report to 18 determine whether chronic inflammation 19 causes ovarian cancer, correct? 20 A. This is my report. 21 Q. And in your report, there's 22 a table that lists each of the 59 slides 23 you have reviewed, correct? 24 A. You mean which page?</p>

<p style="text-align: right;">Page 22</p> <p>1 Q. I don't know the page 2 offhand. But there's a table that you 3 just went through and looked at, correct? 4 A. You mean the -- these 5 tables? 6 Q. Yes, sir. 7 A. Okay. That's what you 8 indicated. 9 Q. Okay. And when you were 10 checking to see if anything was missing, 11 you ran your finger down every one of 12 those slides, didn't you? 13 A. I just want to see whether 14 there's any disruption in the number. 15 Q. Ah. You have those numbers 16 memorized in your head? 17 A. I know this number, but I 18 don't -- but I don't remember the case ID 19 number for each, because this is the 20 data. 21 Q. And so how would you know if 22 there was a slide taken out of that? 23 A. Because there's additions, 24 from 1, 2, 3, 4, 5, to 59, I want to make</p>	<p style="text-align: right;">Page 24</p> <p>1 Q. And I will refer to that 2 with your permission as your expert 3 report? 4 A. Okay. Again, if I'm not 5 clear I will ask you one more time. 6 Q. Okay. In the Exhibit 7 Number 1, the notice to produce, we asked 8 for any and all documents that you have 9 that may pertain to scientific or 10 technical publications, written, prepared 11 or presented by you. Number 7 on Page 6. 12 Do you see that, sir? 13 A. Yes. 14 Q. Have you produced those 15 documents? 16 A. I believe so. 17 Q. Okay. If you would turn to 18 Page 8 and you see a list of requests 19 there starting with authors of any 20 published scientific studies. And then 21 the second one is the Center For 22 Regulatory Effectiveness. 23 Do you see that, sir? 24 A. Yes. B.</p>
<p style="text-align: right;">Page 23</p> <p>1 sure if anything missing in between. 2 Q. Now, sir, have you, in -- in 3 conducting that study -- 4 A. Which study you mean? 5 Q. Well, yes. Let's -- let's 6 discuss your study report to determine 7 whether chronic inflammation causes 8 ovarian cancer. 9 A. You mean this report? 10 Q. Yes, sir. For the -- for -- 11 so that I don't have to name or state 12 that title all day today, would you be 13 comfortable if we referred to that as 14 your study reports? 15 A. If I'm not clear, I will ask 16 one more time. 17 Q. Please do. Thank you. 18 And I will also -- you have 19 also written what we have marked as 20 Exhibit Number 2, an expert report in 21 this litigation, correct? 22 A. You mean this one? 23 Q. Yes. 24 A. Yes. This is my report.</p>	<p style="text-align: right;">Page 25</p> <p>1 Q. Have -- looking down through 2 those, have you had any communication 3 with any of those organizations listed 4 there that is germane to the talcum 5 powder ovarian cancer litigation? 6 A. Could you repeat your 7 question one more time? 8 Q. Looking down through those 9 entities listed there, have you had any 10 communication with any of those 11 organizations that is germane to the 12 talcum powder ovarian cancer litigation? 13 A. Your communications means 14 personal or? 15 Q. Personal. 16 A. Be specific. 17 Q. E-mail, telephone, snail 18 mail, any -- any communication 19 whatsoever. 20 A. No. 21 Q. Now, Number 15 asks for all 22 documents related to research -- I'll 23 wait for you to get there, sir. 24 A. 14?</p>

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<p style="text-align: right;">Page 26</p> <p>1 Q. No, not page. Number, 2 request Number 15. It's on Page 11. 3 A. 11? There's only Page 9. 4 MS. MILLER: I think you 5 must be looking at the responses 6 and he's looking at the requests. 7 He's -- he's got it. 8 BY DR. RESTAINO: 9 Q. Page 9? 10 A. Are you sure, Page 9? 11 Q. Yes, Page 9. My apologies, 12 sir. 13 Number 15 on Page 9. 14 A. Yes. 15 Q. All documents related to 16 research, experiments, testing or any 17 other study that's been done or planned 18 by you which you may rely -- rely upon in 19 the talcum powder litigation. 20 So first, regarding all 21 documents pertaining to experiments that 22 you've performed, you have conducted, as 23 we discussed, and we've called the study 24 report, correct?</p>	<p style="text-align: right;">Page 28</p> <p>1 Q. Well, did you -- if you were 2 looking for the presence or absence of 3 lymphocytes and a particular slide had X 4 number of lymphocytes, did you record 5 that somehow? 6 A. I used the criteria that 7 practicing pathologists used to diagnose 8 chronic inflammation. So those 9 pathologists do not really quantify 10 lymphocytes. It's part of the very basic 11 training for all board-certified 12 pathologists. So I use the same practice 13 for this study. 14 Q. Occasionally, during the day 15 I may ask a question that your attorney, 16 to your left, finds objectionable. And 17 she may say objection. That's for the 18 court, and that's lawyer speak. And 19 occasionally during the day, I may say, 20 "Move to strike nonresponsive," which is 21 sort of my side of the table, my way of 22 saying objection. There's no disrespect 23 meant. 24 I'm going to move to strike</p>
<p style="text-align: right;">Page 27</p> <p>1 A. So -- 2 MS. MILLER: Objection. 3 THE WITNESS: So what do you 4 mean testing? 5 BY DR. RESTAINO: 6 Q. Well, testing, let's use the 7 definition of looking at 8 histopathological slides. 9 In that study report, in 10 looking at the histopathological slides, 11 did you produce any and all documents 12 that pertained to that experiment? 13 A. The documents I produce is 14 the photographs that are shown in my 15 exhibit. 16 Q. When you were sitting at the 17 microscope looking at a particular 18 histopathological slide, did you take any 19 notes on that slide? 20 A. No. 21 Q. Okay. Did you assign that 22 slide a grading system of any sort? 23 A. What do you mean grading 24 system?</p>	<p style="text-align: right;">Page 29</p> <p>1 your previous answer because what I asked 2 you -- and I'll modify it now with what 3 you just said. 4 Using basic 5 histopathological technique that a 6 board-certified pathologist would use 7 when looking at a histopathological slide 8 for the presence of lymphocytes, did you 9 make any recordation of whether or not 10 there were lymphocytes in that slide? 11 MS. MILLER: Objection. 12 THE WITNESS: What do you 13 mean "recordation"? 14 BY DR. RESTAINO: 15 Q. Did you write down any notes 16 regarding that particular slide and the 17 presence of lymphocytes? 18 A. We made the diagnosis based 19 on many informations from the microscopic 20 findings. And we did not write down. 21 Q. When it was -- when that 22 examination of a particular slide, Slide 23 Number 1, the first one you looked at, if 24 there was no lymphocytes noted on that</p>

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<p style="text-align: right;">Page 30</p> <p>1 slide -- on that slide, by the time you 2 got to Slide 59, how do you remember what 3 Slide Number 1 was? 4 A. So the basis is not based on 5 the Case 1 or prior cases. It's based on 6 the knowledge, the training. And I am a 7 pathologist, practicing and doing 8 research for 20 years. And I am the 9 Richard TeLinde distinguished research 10 professor in gynecology pathology, which 11 is probably only one in the professorship 12 in the United States. 13 And this professorship is 14 regarded as the most premium position in 15 the country. So I trained so many 16 pathologists, and I practice 17 pathologists. I don't need to write down 18 every single details of pathology 19 findings. And we only need what we need, 20 is the final diagnosis. That does 21 matter. 22 Everything is computing in 23 our brain to come up with the conclusion 24 and the final diagnosis without going to</p>	<p style="text-align: right;">Page 32</p> <p>1 So it based on two things. 2 One is architecture of the histology, the 3 relationship between the epithelial cells 4 different, microenvironment, 5 extracellular cells, the architecture, 6 number one. 7 But it's not sufficient, 8 okay, for the final diagnosis. That is 9 required. The second important thing is 10 cytology. Cytology means the 11 morphological features of the single 12 cells or group of cells. 13 And we look at the nucleus, 14 if it is benign, or normal, usually they 15 are more homogenous. Okay. It looks 16 very similar to -- to the neighboring 17 cells. But in cancer, in cancer, you 18 will see a lot of different things, we 19 call nuclear -- 20 Q. Sir, I'm going to have to 21 interrupt you now. I'm going to make a 22 motion to strike as unresponsive, because 23 all I asked you is not the technique that 24 a board-certified pathologist may or may</p>
<p style="text-align: right;">Page 31</p> <p>1 any details. Lymphocytes, plasma cells, 2 and, like, NK cells, epithelial cells, 3 and how many blood vessels, how many red 4 blood cells, white blood cells, how many 5 fibroblasts, and how many epithelial 6 cells. 7 This is not our basis. Our 8 basis is to take into -- take the whole 9 thing into the final decision. Every -- 10 we can consider every aspect and come to 11 our final diagnosis, rather than based on 12 single lymphocytes, endothelial cells, 13 and morphological features. 14 So basically, I think this 15 is very important for non-pathologists or 16 nonmedical doctors to understand, how do 17 we make the diagnosis of pathology. 18 So pathology -- what we 19 meant pathology, like, when you have a 20 tumor, whether is it benign or malignant, 21 it's very important, right? You know, 22 your nevus -- could there -- this a 23 melanoma that will kill you, or is it 24 benign nevus, and you are fine?</p>	<p style="text-align: right;">Page 33</p> <p>1 not use, but when a pathologist is 2 looking at a large number -- God bless 3 you -- large number of slides, and in 4 this case, 59 slides, without recording, 5 making notes of the number, the 6 quantitative analysis of each slide of 7 the number of lymphocytes, how can you 8 remember when you're all done with your 9 analysis, the total number that are 10 present in each slide? 11 A. Sir, I need to give you the 12 complete and full answer; otherwise, you 13 will not understand how the pathologist 14 made the diagnosis. So if you don't 15 listen to that, you can never understand 16 what your pathology doctor diagnose your 17 tumor or your lesions -- 18 Q. Okay. 19 A. -- of course, if you had 20 one. 21 Q. We will discuss that in 22 detail, then, when we get to your study 23 report -- 24 A. Okay.</p>

<p style="text-align: right;">Page 34</p> <p>1 Q. -- and go through the 2 methodology that you employed at that 3 time. 4 Now, Doctor, you were -- you 5 provided deposition testimony in a number 6 of cases involving transvaginal mesh, 7 correct? 8 A. That's -- I remember. 9 Q. Okay. And were you an 10 expert at that time for C.R. Bard 11 Incorporated and Ethicon Incorporated? 12 MS. MILLER: Objection. 13 THE WITNESS: Could you 14 repeat the companies' names? 15 BY DR. RESTAINO: 16 Q. First, C.R. Bard. Does that 17 sound familiar? 18 A. Okay. How about the other 19 one? 20 Q. Ethicon. 21 A. Yes, I remember. 22 Q. And you were an expert for 23 the defense, correct? 24 MS. MILLER: Objection.</p>	<p style="text-align: right;">Page 36</p> <p>1 transvaginal mesh, did you testify on 2 behalf of any woman? 3 MS. MILLER: Objection. 4 THE WITNESS: I testified my 5 pathology findings. 6 BY DR. RESTAINO: 7 Q. As an expert for C.R. Bard 8 or Ethicon, correct? 9 MS. MILLER: I think these 10 are -- 11 THE WITNESS: I think I 12 answer -- 13 MS. MILLER: Objection. 14 THE WITNESS: -- your 15 question. 16 MS. MILLER: I think these 17 are legal terms. I think Dr. Shih 18 is a pathologist. Dr. Shih is not 19 a native English speaker. And I 20 don't think it's fair to ask him 21 trick questions. 22 DR. RESTAINO: We're going 23 to have a nice depo today. We're 24 not going to have speaking</p>
<p style="text-align: right;">Page 35</p> <p>1 THE WITNESS: I was asked as 2 a pathology expert to look at the 3 slides, whether there is any 4 evidence of abnormality on the 5 tissues. 6 I did not give any opinion 7 outside my pathology expertise. 8 BY DR. RESTAINO: 9 Q. Okay. Did you -- in the 10 transvaginal mesh litigation, have you 11 ever testified on behalf of a woman 12 instead of the company? 13 MS. MILLER: Objection. 14 THE WITNESS: Could you 15 repeat the question one more time? 16 BY DR. RESTAINO: 17 Q. In the transvaginal mesh 18 litigation, were you ever retained as an 19 expert on behalf of one of the 20 plaintiffs, one of the women, complaining 21 of morbidity associated with her mesh? 22 A. In which case? Bard or -- 23 Q. Either one or any other 24 case. Have you ever -- in the</p>	<p style="text-align: right;">Page 37</p> <p>1 objections. Those are, 2 "Objection." 3 BY DR. RESTAINO: 4 Q. Doctor -- 5 MS. MILLER: No, that is not 6 fair. He obviously doesn't 7 understand your question. And 8 you're purposely trying to trick 9 him. And that's just not 10 appropriate. 11 BY DR. RESTAINO: 12 Q. Doctor, have you -- in the 13 transvaginal mesh litigation, were you 14 retained by any lawyer that represents 15 any of the women harmed by transvaginal 16 mesh? Do you understand that question? 17 MS. MILLER: Objection. 18 THE WITNESS: I cannot 19 understand the question. 20 MS. MILLER: Lacks 21 foundation. 22 BY DR. RESTAINO: 23 Q. Okay. Did you write expert 24 report as an expert in the transvaginal</p>

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<p>1 mesh?</p> <p>2 A. I report the pathology</p> <p>3 finding under microscope, whether the</p> <p>4 tissue has foreign body material or</p> <p>5 anything that I can show in my report, I</p> <p>6 report it.</p> <p>7 Q. Did you make an analysis of</p> <p>8 whether that pathology was due to the</p> <p>9 presence of mesh?</p> <p>10 A. I think I defer to clinician</p> <p>11 for this question.</p> <p>12 Q. Okay. When were you first</p> <p>13 contacted to be an expert in this current</p> <p>14 litigation, the talcum powder litigation?</p> <p>15 A. I think it's in the end</p> <p>16 December 2018.</p> <p>17 Q. And who first contacted you?</p> <p>18 A. I think who was Johnson &</p> <p>19 Johnson attorney firm.</p> <p>20 Q. And do you know the name of</p> <p>21 the lawyer who first contacted you?</p> <p>22 A. Who was Jessica.</p> <p>23 Q. Okay. Have you worked with</p> <p>24 Jessica before?</p>	<p>1 testified that he didn't talk to</p> <p>2 me till December.</p> <p>3 DR. RESTAINO: Well, we've</p> <p>4 had some confusion with some</p> <p>5 answers, so I just want to make</p> <p>6 sure, from two different ways,</p> <p>7 that, in fact, he wasn't working</p> <p>8 for them in November.</p> <p>9 BY DR. RESTAINO:</p> <p>10 Q. Did you see any expert</p> <p>11 reports from any of the plaintiffs in</p> <p>12 November of 2018?</p> <p>13 MS. MILLER: Same objection.</p> <p>14 Mischaracterizes the plaintiff's</p> <p>15 testimony and further efforts to</p> <p>16 try to confuse somebody who is not</p> <p>17 a native English speaker.</p> <p>18 BY DR. RESTAINO:</p> <p>19 Q. Did you understand my</p> <p>20 question?</p> <p>21 A. Could you repeat one more</p> <p>22 time?</p> <p>23 Q. The expert report of</p> <p>24 Dr. Sarah Kane, did you see that expert</p>
Page 39	Page 41
<p>1 A. I don't remember.</p> <p>2 Q. Did you work with Jessica,</p> <p>3 for example, in the transvaginal mesh</p> <p>4 litigation?</p> <p>5 A. I did not.</p> <p>6 Q. And when you first met with</p> <p>7 Jessica, what were you asked to do?</p> <p>8 MS. MILLER: Objection.</p> <p>9 Please don't reveal any of our</p> <p>10 privileged conversations. Any</p> <p>11 conversation that you and I had is</p> <p>12 privileged.</p> <p>13 BY DR. RESTAINO:</p> <p>14 Q. That -- that's a fair</p> <p>15 objection. Let me strike the question.</p> <p>16 I'll represent to you that</p> <p>17 the expert reports on behalf of the</p> <p>18 plaintiff, so for example Dr. Sarah Kane,</p> <p>19 Dr. Saed, those reports were produced to</p> <p>20 the defense counsel and the courts on --</p> <p>21 in mid November of 2018.</p> <p>22 Did you see those expert</p> <p>23 reports in November of 2018?</p> <p>24 MS. MILLER: Objection. He</p>	<p>1 report in November of 2018?</p> <p>2 A. I first know about this</p> <p>3 litigation after December.</p> <p>4 Q. Now, prior to your</p> <p>5 deposition today, and prior to being --</p> <p>6 to meeting with Jessica, did you ever</p> <p>7 meet with any plaintiffs' lawyers?</p> <p>8 A. Who are the plaintiffs'</p> <p>9 lawyers?</p> <p>10 Q. The defense lawyers are</p> <p>11 sitting on your side of the table. The</p> <p>12 lawyers here are the plaintiff lawyers,</p> <p>13 in addition to others who are not here.</p> <p>14 A. I do not remember their</p> <p>15 faces.</p> <p>16 Q. Okay. Do you remember the</p> <p>17 lovely lady sitting to my right, Michelle</p> <p>18 Parfitt?</p> <p>19 A. I cannot recognize your</p> <p>20 faces.</p> <p>21 MS. PARFITT: I've aged.</p> <p>22 THE WITNESS: I hope not.</p> <p>23 BY DR. RESTAINO:</p> <p>24 Q. Do you recall meeting with</p>

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<p style="text-align: right;">Page 42</p> <p>1 Ms. Parfitt in 2015?</p> <p>2 A. I cannot remember that.</p> <p>3 Q. Do you remember having any</p> <p>4 conversations with a female lawyer in</p> <p>5 2015 regarding talcum powder and ovarian</p> <p>6 cancer?</p> <p>7 A. I cannot remember at all.</p> <p>8 Q. Do you -- do you recall</p> <p>9 informing any female attorney in 2015</p> <p>10 that in order to render an expert opinion</p> <p>11 regarding talcum powder and ovarian</p> <p>12 cancer, you would need to do a rat study?</p> <p>13 A. Rat study?</p> <p>14 Q. Yes.</p> <p>15 A. I cannot remember that</p> <p>16 either.</p> <p>17 Q. Okay. Do you have -- do --</p> <p>18 when you meet with lawyers, do you</p> <p>19 typically charge the lawyers for your</p> <p>20 time?</p> <p>21 A. I think that's correct.</p> <p>22 Q. And would you have any</p> <p>23 record of receiving money from</p> <p>24 Ms. Parfitt or -- or the law firm</p>	<p style="text-align: right;">Page 44</p> <p>1 the record to talk about it?</p> <p>2 MS. SHARKO: Do you want to</p> <p>3 step out in the hall and you can</p> <p>4 explain it to me?</p> <p>5 MS. PARFITT: No, actually</p> <p>6 I'd like to continue the</p> <p>7 deposition. We can take a break</p> <p>8 at another time. I'd like to</p> <p>9 continue with the doctor's</p> <p>10 deposition.</p> <p>11 MS. SHARKO: You can go</p> <p>12 ahead with the deposition, but I</p> <p>13 think this is kind of unfair. But</p> <p>14 proceed.</p> <p>15 MS. PARFITT: Well, I'm</p> <p>16 just -- I think when we continue</p> <p>17 to talk with the doctor, I don't</p> <p>18 think you'll find anything unfair.</p> <p>19 The doctor doesn't remember</p> <p>20 speaking to me. Again, I'm not</p> <p>21 being examined.</p> <p>22 BY DR. RESTAINO:</p> <p>23 Q. Dr. Shih, if you checked</p> <p>24 your checking account or savings account</p>
<p style="text-align: right;">Page 43</p> <p>1 Ashcraft Gerel in 2015 or -- or 2016?</p> <p>2 A. I cannot recall that.</p> <p>3 Q. If you did, when you do</p> <p>4 receive money from attorneys or a law</p> <p>5 firm for medical/legal consultation, for</p> <p>6 example now from Johnson & Johnson, does</p> <p>7 the money go to you directly or does it</p> <p>8 go to a particular fund at Johns Hopkins</p> <p>9 or elsewhere?</p> <p>10 A. If I receive a check with my</p> <p>11 name, it come to me.</p> <p>12 Q. Would you --</p> <p>13 MS. MILLER: And, Michelle,</p> <p>14 this is all new to us. If there</p> <p>15 is a conflict issue that you're</p> <p>16 raising, I -- I submit you should</p> <p>17 have brought this to our attention</p> <p>18 many months ago.</p> <p>19 MS. PARFITT: We can talk</p> <p>20 about it off the record. I'm not</p> <p>21 being examined now. We can talk</p> <p>22 about it. I need to hear what the</p> <p>23 doctor has to say.</p> <p>24 MS. MILLER: Shall we go off</p>	<p style="text-align: right;">Page 45</p> <p>1 for any deposits in 2015 or 2016 from a</p> <p>2 law firm would you be able to determine</p> <p>3 that you received money for that</p> <p>4 consultation?</p> <p>5 A. I need to study this.</p> <p>6 Q. Okay. Thank you.</p> <p>7 Prior to meeting with</p> <p>8 Jessica in the end of December of 2018 --</p> <p>9 MS. MILLER: Objection. He</p> <p>10 did not testify that he met with</p> <p>11 me in the end of December of 2018.</p> <p>12 He testified that I contacted him.</p> <p>13 That's mischaracterizing the</p> <p>14 testimony.</p> <p>15 BY DR. RESTAINO:</p> <p>16 Q. When -- when Jessica</p> <p>17 contacted you in December of 2018, before</p> <p>18 you agreed to become -- to -- to work as</p> <p>19 an expert on behalf of Johnson & Johnson,</p> <p>20 did you need to approach the Johns</p> <p>21 Hopkins University ethics department for</p> <p>22 permission?</p> <p>23 A. I don't think there's a</p> <p>24 guideline for that. I would need to</p>

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<p style="text-align: right;">Page 46</p> <p>1 report is so-called outside activity. So</p> <p>2 we report all the outside activity, like</p> <p>3 consultation and expert witness and we</p> <p>4 disclose it to our system. And that's</p> <p>5 it. And I did.</p> <p>6 Q. In order to conduct what we</p> <p>7 have marked as Exhibit Number 4 and</p> <p>8 agreed to refer to as your study report,</p> <p>9 did you have to obtain permission from</p> <p>10 Johns Hopkins University or any other</p> <p>11 entity to conduct that study?</p> <p>12 MS. MILLER: Objection.</p> <p>13 THE WITNESS: Can I give you</p> <p>14 the complete answer?</p> <p>15 BY DR. RESTAINO:</p> <p>16 Q. It's a yes or no. Did you</p> <p>17 have to -- did you contact Johns Hopkins</p> <p>18 University about conducting this study?</p> <p>19 A. This study is part of our</p> <p>20 basic research and our whole team</p> <p>21 starting from 2012. And this study is in</p> <p>22 continuation of our 2014, if I can</p> <p>23 remember correctly, from Ardighieri study</p> <p>24 published in International Journal of GYN</p>	<p style="text-align: right;">Page 48</p> <p>1 just coincidental that we have this</p> <p>2 research going on. And when I was</p> <p>3 involved in reviewing the articles and</p> <p>4 plaintiff material, et cetera, and I feel</p> <p>5 one of the most important question to be</p> <p>6 answered is the precursor lesions, which</p> <p>7 is the -- where the ovarian high grade</p> <p>8 serous carcinoma originate.</p> <p>9 And so this one issue,</p> <p>10 whether there is chronic inflammation</p> <p>11 involved in this carcinogenesis of high</p> <p>12 grade ovarian cancer, is that right? So</p> <p>13 that is why I think our current study</p> <p>14 will be able to provide cogent evidence</p> <p>15 to show or -- or to not show, meaning</p> <p>16 refute or support.</p> <p>17 I don't have any pre-set</p> <p>18 mind whether chronic inflammation is</p> <p>19 present in the early precursor ovarian</p> <p>20 cancer lesions. So that's my purpose.</p> <p>21 Q. Sir, you're going to have to</p> <p>22 ask -- listen to my question carefully</p> <p>23 and I'll repeat it as -- as many times as</p> <p>24 you need for me to repair it -- repeat</p>
<p style="text-align: right;">Page 47</p> <p>1 Pathology. And this is the continuation</p> <p>2 of a study. It is not particularly for</p> <p>3 this litigation, and my opinion is not</p> <p>4 dependent on this study. And so this</p> <p>5 study is only part of our ongoing</p> <p>6 research in answering what is the</p> <p>7 pathogenesis in initiating high grade</p> <p>8 ovarian serous carcinoma.</p> <p>9 And as you know, there's</p> <p>10 different types of ovarian cancer. In</p> <p>11 this study we only focus on, as this</p> <p>12 chart, I think it's useful for my</p> <p>13 explanation, is a high grade serous</p> <p>14 carcinoma. So that is one of our major</p> <p>15 focus's point.</p> <p>16 Q. Okay. This is the</p> <p>17 Department of Defense grant that you're</p> <p>18 referring to; is that correct?</p> <p>19 A. Correct.</p> <p>20 Q. Did you have to obtain</p> <p>21 permission from anyone involved with that</p> <p>22 grant to conduct this study?</p> <p>23 A. Again, to conduct this study</p> <p>24 is not for this litigation purpose. It</p>	<p style="text-align: right;">Page 49</p> <p>1 it. I'm going to move to strike as</p> <p>2 unresponsive because my question, sir,</p> <p>3 was did you have to obtain permission</p> <p>4 from anyone that -- involved in that</p> <p>5 grant in order to conduct what you just</p> <p>6 described as a continuing study from that</p> <p>7 grant?</p> <p>8 A. So as a scientist, we</p> <p>9 publish papers. We don't need to report</p> <p>10 every time to the grant -- grant agency,</p> <p>11 NIH or DOD, to afford permission. This</p> <p>12 is the freedom of academia.</p> <p>13 Q. Okay. And that grant</p> <p>14 involves millions of dollars, does it</p> <p>15 not?</p> <p>16 A. For many investigators and</p> <p>17 many institutions.</p> <p>18 Q. Now, for the time that you</p> <p>19 spent developing the methodology that you</p> <p>20 were going to employ to do the study, for</p> <p>21 the time spent looking at -- looking at</p> <p>22 the histopathological slides, for the</p> <p>23 time spent writing your study report, are</p> <p>24 you billing the grant for that time?</p>

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<p style="text-align: right;">Page 50</p> <p>1 A. The grant has expired, okay. 2 So my research on this is supported by my 3 own time. 4 Q. Are you -- did you bill or 5 will you bill anyone representing Johnson 6 & Johnson for the time you spent 7 developing the methodology for the study, 8 reviewing the histopathological slides, 9 and writing your expert report? 10 A. I will not. 11 Q. So all of that time that 12 you've spent, you will not be reimbursed 13 for -- from anyone for that time; is that 14 correct? 15 A. Anyone means? 16 Q. Any -- the university, any 17 other grant money, any other entity. 18 Will anybody be paying you for that time 19 that you spent? 20 A. Sir, you need to understand, 21 when we do a research, every research, 22 okay, there's many publications. We 23 report it. We did not charge each 24 publication to any agency, no, we are</p>	<p style="text-align: right;">Page 52</p> <p>1 study? 2 MS. MILLER: Objection. 3 Asked and answered. 4 He said he wasn't. 5 THE WITNESS: I did answer 6 your question very clearly. 7 BY DR. RESTAINO: 8 Q. Your answer is no? 9 A. I already answered your 10 question. 11 Q. Okay. Sir, do you consider 12 yourself an expert in epidemiology? 13 A. I am a cancer biologist who 14 focus on -- I understand what initiate 15 ovarian cancer, and I am also practicing 16 gynecology pathologist. And I also 17 run -- educator to train residents, 18 pathology residents, post-doc fellows, 19 and the graduate students in ovarian 20 cancer research and diagnosis. 21 Q. Do you have expertise in 22 epidemiology? 23 A. As a scientist, I always 24 review epidemiology literatures. It's</p>
<p style="text-align: right;">Page 51</p> <p>1 not. We are paid by the fixed salary to 2 do this, to do all the academic research, 3 education, clinical practice, and 4 administration. 5 This is just part of the 6 academia success in the United States. 7 You cannot break into every single one. 8 For example, I interview 9 with a faculty. I charge the 10 institution. We did not do it that way. 11 So this is totally different for other 12 business. 13 In academia -- let me 14 finish. This is very important. We are 15 the scientists. We are here to do 16 education, clinical practice, research 17 for the benefit of all the women in whole 18 wide world for ovarian cancer. 19 Q. Sir, again, I have to 20 interrupt you. I'm going to move to 21 strike as unresponsive. My simple 22 question is, are you billing anyone for 23 the time you spent designing, conducting, 24 and writing up your report from that</p>	<p style="text-align: right;">Page 53</p> <p>1 part of my background to study it, the 2 issue. And also it's in my context. 3 So you cannot say a 4 scientist only focus on biology without 5 knowing the other fields. I don't think 6 it will work. Any great scientist shall 7 not do that. They should review all the 8 literatures related. 9 Q. I'm sorry, sir. 10 A. Sorry. 11 Q. And by reviewing the 12 published literature dealing with 13 epidemiology, does that give you 14 expertise in epidemiology? 15 MS. MILLER: Objection. 16 THE WITNESS: As I said, I 17 reviewed other literatures in 18 order to know better about the 19 issues, about the -- what is the 20 origin of ovarian cancer. 21 And it is a background in my 22 study and also in my context. 23 BY DR. RESTAINO: 24 Q. Okay. Do you have expertise</p>

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<p>1 in toxicology?</p> <p>2 A. Again, I'm a cancer</p> <p>3 biologist and gynecology pathologist.</p> <p>4 Q. Okay. Do you have expert --</p> <p>5 expertise in mineralogy?</p> <p>6 A. How do you define</p> <p>7 mineralogy?</p> <p>8 Q. How would you define</p> <p>9 mineralogy?</p> <p>10 MS. MILLER: Objection.</p> <p>11 THE WITNESS: Because I</p> <p>12 can't understand your word. Could</p> <p>13 you explain that.</p> <p>14 BY DR. RESTAINO:</p> <p>15 Q. The study of minerals, for</p> <p>16 example talc and asbestos.</p> <p>17 A. Ah.</p> <p>18 Q. Are you an expert?</p> <p>19 A. No, I am not.</p> <p>20 Q. Do you consider you're an</p> <p>21 expert in talcum powder products?</p> <p>22 MS. MILLER: Objection.</p> <p>23 THE WITNESS: Could you be</p> <p>24 more specific for the question?</p>	<p>1 Q. Today.</p> <p>2 A. Today, I did not see any</p> <p>3 Johnson & Johnson's powder.</p> <p>4 Q. Okay. Have you heard of Sir</p> <p>5 Austin Bradford Hill?</p> <p>6 A. Could you spell the name</p> <p>7 correctly?</p> <p>8 Q. Sir Austin Bradford Hill.</p> <p>9 Have you heard of him?</p> <p>10 A. I saw -- I know the</p> <p>11 documents -- I know the documents. Okay.</p> <p>12 Through this kind of expert opinion,</p> <p>13 investigation, and I -- I remember I saw</p> <p>14 that document, but I cannot remember any</p> <p>15 single word.</p> <p>16 Q. Did you conduct an analysis</p> <p>17 in this case utilizing the Bradford Hill</p> <p>18 viewpoints on causation?</p> <p>19 A. Again, can I have this Brad</p> <p>20 Hill -- Bradford Hill documents before we</p> <p>21 can further discuss?</p> <p>22 Q. I'm not sure what you mean</p> <p>23 by the Bradford Hill documents. But do</p> <p>24 you recall reading at any time in your</p>
Page 55	Page 57
<p>1 BY DR. RESTAINO:</p> <p>2 Q. Are you familiar with talcum</p> <p>3 powder products?</p> <p>4 MS. MILLER: Objection.</p> <p>5 THE WITNESS: What do you</p> <p>6 mean familiar with?</p> <p>7 BY DR. RESTAINO:</p> <p>8 Q. Do you know what is in, for</p> <p>9 example, bottles of Johnson & Johnson</p> <p>10 talcum powder?</p> <p>11 A. I think you have several</p> <p>12 questions in a stream. Could you --</p> <p>13 might go by steps, your question, one by</p> <p>14 one by one, so I can answer your question</p> <p>15 more effectively.</p> <p>16 Q. Do you know what the</p> <p>17 constituent parts of Johnson & Johnson's</p> <p>18 talcum powder is or are?</p> <p>19 A. You mean the Johnson &</p> <p>20 Johnson's powder in the market?</p> <p>21 Q. Yes.</p> <p>22 A. Or in -- back to ten years</p> <p>23 ago, 20 years ago, 30 years ago? What do</p> <p>24 you mean?</p>	<p>1 professional career a 1965 publication by</p> <p>2 Sir Bradford Hill regarding viewpoints</p> <p>3 for determining causation?</p> <p>4 A. Can I see the viewpoints for</p> <p>5 our discussion?</p> <p>6 Q. I just want to know if you</p> <p>7 recall seeing that paper.</p> <p>8 A. I need to see the paper in</p> <p>9 order to answer your question.</p> <p>10 Q. Do you recall anytime</p> <p>11 reading a published paper dealing with</p> <p>12 causation and viewpoints that consisted</p> <p>13 of, for example, the strength of</p> <p>14 association, analogy, biological</p> <p>15 gradient, biological plausibility,</p> <p>16 analogy, experimentation, and coherence?</p> <p>17 Do you recall ever seeing any document</p> <p>18 like that?</p> <p>19 MS. MILLER: Objection.</p> <p>20 Compound.</p> <p>21 THE WITNESS: I need to see</p> <p>22 the documents before we can</p> <p>23 further discuss.</p> <p>24 BY DR. RESTAINO:</p>

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<p>1 Q. Without seeing any document, 2 you can't recall ever reading or seeing a 3 study or publication dealing with 4 viewpoints of causation? 5 A. I saw the viewpoint, but I 6 need to see documents to see which ones 7 specifically you refer. 8 Q. When you were doing your 9 analysis of the published literature and 10 your study report to make a determination 11 as to whether or not the Johnson & 12 Johnson's talcum powder products were 13 associated with any form of ovarian 14 cancer, did you go through a list of 15 viewpoints to determine whether the 16 association was causal? 17 MS. MILLER: Objection. 18 You -- you -- 19 DR. RESTAINO: Objection 20 works. 21 MS. MILLER: There's no 22 foundation. This mischaracterizes 23 his testimony. These questions 24 are really not fair.</p>	<p>1 objection or we're going to call 2 the judge. 3 MS. SHARKO: Okay. 4 DR. RESTAINO: We can fight 5 about it over another time. I'm 6 trying to be clear as I can for 7 someone whose English is a second 8 language. I know that and I 9 respect it. 10 BY DR. RESTAINO: 11 Q. Doctor -- 12 MS. MILLER: Your question 13 embedded an entire assumption that 14 had never been made in this 15 deposition, that had never been 16 accepted by the witness. And I 17 think that's hard for somebody to 18 understand who doesn't -- who is 19 not -- English -- who does not 20 speak English as a first language. 21 So I'm just asking to please 22 keep the questions to 23 straightforward questions that 24 don't embed false assumptions.</p>
Page 59	Page 61
<p>1 When did he say that he did 2 an analysis of the published 3 literature and a study report to 4 make a determination as to whether 5 not Johnson & Johnson's talcum 6 powders were associated with any 7 ovarian -- form of ovarian cancer? 8 I'm sorry to be giving 9 speaking objections, but as I 10 said, this gentleman is a 11 scientist. He is not a native 12 English speaker, and I think the 13 questions should be fair. 14 DR. RESTAINO: Your 15 objection is noted. Let's keep it 16 to objection. They are the 17 federal rules. 18 MS. MILLER: I'll say 19 objection unless I feel that the 20 question is stated in such a way 21 that it is intended to mislead 22 this witness. 23 DR. RESTAINO: Actually 24 you're going to keep it to</p>	<p>1 BY DR. RESTAINO: 2 Q. Doctor, if you would turn in 3 your expert report which is marked as 4 Exhibit Number 2 and turn to Page 11. 5 And now, there's a figure there. Figure 6 Number 2 on Page 11, correct? 7 A. Correct. 8 Q. And right above that, 9 there's a sentence where you write, 10 "Without this direct molecular pathology 11 evidence," do you see where I am, sir? 12 A. I'm sorry, where are you? 13 Q. The sentence right above the 14 figure. 15 A. Okay. Okay. I saw it. 16 Q. "Without this direct 17 molecular pathology evidence, a causal 18 relationship of talc and ovarian cancer 19 cannot be established (see below)." 20 Do you see that, sir? 21 A. Let me finish the whole 22 section, okay. 23 Q. No, sir. I just want to 24 know if you -- if you can see that</p>

<p style="text-align: right;">Page 62</p> <p>1 sentence that I just read. 2 A. Okay. 3 Q. Do you see that, sir? 4 MS. SHARKO: He's just 5 directing your attention to that 6 sentence. 7 THE WITNESS: Oh, okay, 8 yeah, I saw the sentence you -- 9 BY DR. RESTAINO: 10 Q. You see the sentence. 11 A. -- you mentioned. 12 Q. And it is your expert 13 opinion, is it not, that without direct 14 molecular pathology evidence, a causal 15 relationship of talc and ovarian cancer 16 cannot be established; is that correct? 17 A. I think any cancer biologist 18 will agree that you need to see the 19 genetic mutation in order to establish 20 causal relationship. As you know, the 21 cancer biology, cancer origin is based on 22 genetics, and cancer is a genetic 23 disease. It must have mutations. 24 There's a difference between cancer and</p>	<p style="text-align: right;">Page 64</p> <p>1 methodology to support biological 2 plausibility and the mechanism. 3 And mutation is one of them, is 4 one of them. 5 BY DR. RESTAINO: 6 Q. Do you recall in any of your 7 readings the statement that -- regarding 8 biological plausibility? Are you 9 familiar with that term? 10 A. Could you define your 11 definition? I don't know which 12 biological plausibility you refer to. 13 Q. I'm not referring to any 14 specific form of biological plausibility. 15 You as an expert, can you define for us 16 what is meant by biological plausibility? 17 A. Okay. In my opinion, 18 biological plausibility is the evidence, 19 based on very good methodology, that can 20 support a statement. For example, talc 21 is causal to ovarian cancer. 22 Q. And is it biologically 23 plausible in your mind as an expert that 24 talc, talcum powder, is associated with</p>
<p style="text-align: right;">Page 63</p> <p>1 normal cells. 2 So in order to understand 3 the sentence I wrote, you need to 4 understand that cancer is just not coming 5 from nowhere. It has a basis of 6 molecular genetic changes, including 7 somatic mutations in cancer driver genes, 8 which is in contrast to cancer mutational 9 genes. And the cell, this is the origin 10 that every cancer can -- can develop. 11 Without mutations, there's no way that 12 you can say that this is the -- the 13 causal. 14 Q. Okay. So is it your expert 15 opinion that before a causal relationship 16 between an environmental agent and cancer 17 can be established, you have to see 18 evidence of direct molecular pathology? 19 MS. MILLER: Objection. 20 Mischaracterizes the witness's 21 testimony. 22 THE WITNESS: What I said is 23 you need to have cogent evidence 24 and credible science and</p>	<p style="text-align: right;">Page 65</p> <p>1 ovarian cancer? 2 MS. MILLER: Objection. He 3 said causal, you're saying 4 association. 5 THE WITNESS: I said causal. 6 You say association. I don't mean 7 association. 8 Association doesn't mean 9 it's causal. It is a very basic 10 scientific logic, everybody should 11 know that. 12 BY DR. RESTAINO: 13 Q. Would you -- do you agree 14 that the biological plausibility depends 15 upon the science of the day, would you 16 agree? 17 A. That's too general. I 18 cannot answer that. If you have more 19 specific, give me an example, then I can 20 give you an answer. 21 Q. Would you agree that science 22 is a continuum and what scientists know 23 one year from now might be different from 24 what scientists know today?</p>

<p style="text-align: right;">Page 66</p> <p>1 A. It depends on what kind of 2 science. Only true science will survive. 3 Q. Okay. Would you -- do you 4 agree that research is never finished, 5 but carries on and on? 6 MS. MILLER: Objection. 7 THE WITNESS: This is too 8 general. I don't know what this 9 means. 10 MS. MILLER: Doctor, please 11 remember to give me ten seconds -- 12 THE WITNESS: Okay. 13 MS. MILLER: -- between his 14 question and your answer so that I 15 can lodge my objection and the 16 record is clear. 17 BY DR. RESTAINO: 18 Q. And I'm sorry, regarding 19 research, would you agree that research 20 never is finished? 21 MS. MILLER: Objection. 22 Vague. 23 THE WITNESS: Is too vague a 24 question. I cannot answer that.</p>	<p style="text-align: right;">Page 68</p> <p>1 causal or not. 2 Q. And you looked, did you not, 3 at various epidemiological studies 4 looking at the association of talcum 5 powder and ovarian cancer, correct? 6 A. I study some of them. 7 Q. In fact, if you look in your 8 expert report on Page 11? 9 A. Yes, I saw it. 10 Q. Okay. Are you on Page 11? 11 A. Yes, I am -- I think so. 12 Q. Do you see there on -- on 13 Page 11 a description of epidemiological 14 studies that you reviewed? 15 A. Which -- which line you are 16 talking about? Which study? Could you 17 name the first author of the study and 18 year? 19 Q. On the -- on the bottom of 20 Page 11, you have a numbered paragraph, 21 Number 4, correct? 22 A. Yes. 23 Q. Do you see there where 24 you've written, "A number of</p>
<p style="text-align: right;">Page 67</p> <p>1 BY DR. RESTAINO: 2 Q. You don't understand what I 3 mean by asking -- 4 A. It's too vague. It's not -- 5 I cannot understand. 6 Q. Are you familiar -- familiar 7 with basic epidemiological principles? 8 A. What do you mean basic 9 principle? It's too general. 10 Q. Do you know how, when 11 looking at a study that has some degree 12 of epidemiology in it, do you know how to 13 interpret a confidence interval? 14 A. Again, I'm a cancer 15 biologist and a gynecology pathologist. 16 I review those articles that is relevant 17 and important and -- and related. I am 18 not epidemiology expert. You can -- you 19 should defer those question to them. I 20 can -- I am here -- okay. This is very 21 important. 22 My job here is served as an 23 expert in cancer biology and gynecology 24 pathology to answer whether talc is -- is</p>	<p style="text-align: right;">Page 69</p> <p>1 epidemiological studies clearly fail to 2 show an association between talc exposure 3 and women who develop ovarian cancer 4 including prospective cohort studies 5 (Houghton, et al., 2014; Gertig, et al., 6 2000; Gates, et al., 2010; Gonzalez et 7 al., 2016)?" 8 Do you see that, sir? 9 A. Yes, I did. 10 Q. Now, you reviewed those 11 studies? 12 A. I reviewed the study quickly 13 and come to my report. But I -- I should 14 say I reviewed those articles and not 15 only these four, but several here. So I 16 just come up with my general opinion as a 17 sum, as a cancer biological view, like a 18 bird's-eye-view about epidemiology. I 19 cannot give you the full-blown -- and the 20 details about a specific study. 21 So what I feel after I 22 review this, Gertig, Gates, Gonzalez, 23 Houghton, and several others perhaps, my 24 thinking is number one, those</p>

<p style="text-align: right;">Page 70</p> <p>1 epidemiology studies did not show 2 consistent result. For example, as you 3 know, there are two basic epidemiology 4 studies. One is longitudinal cohort -- 5 okay, cohort. 6 MS. SHARKO: Dr. Shih, I'm 7 going to interrupt you to help 8 Mr. -- Dr. Restaino out. He just 9 wants to know if you looked at 10 those studies. And so -- 11 THE WITNESS: Okay. Thank 12 you very much. 13 DR. RESTAINO: Thank you. 14 MS. SHARKO: That's his 15 question. Then he's going to ask 16 you another question. 17 THE WITNESS: Okay. Yes, I 18 reviewed those studies. 19 BY DR. RESTAINO: 20 Q. When you -- 21 MS. MILLER: Is this -- oh, 22 sorry. 23 DR. RESTAINO: I'm sorry. 24 Go ahead.</p>	<p style="text-align: right;">Page 72</p> <p>1 weaknesses of each epidemiological study, 2 would you defer to someone who has 3 expertise and a degree in epidemiology? 4 MR. LOCKE: Objection to 5 form. 6 MS. MILLER: Objection. 7 THE WITNESS: If the 8 strength is really high, like a 9 20, 30, like cigarette smoking, I 10 think everybody will accept that's 11 a risk factor. 12 If really low, like 1.5, 13 below, 1.1, it could be just by 14 chance and that's needed expert -- 15 experts to look into that to study 16 the confounding factors, case 17 number and et cetera, et cetera. 18 BY DR. RESTAINO: 19 Q. When you are writing an 20 academic paper for publication, any 21 paper, do you typically conduct a review 22 of the literature for articles germane to 23 the paper you were going to write? 24 A. I will cite many papers that</p>
<p style="text-align: right;">Page 71</p> <p>1 MS. MILLER: I think we've 2 gone an hour. I think we could 3 all use a bathroom break. Is this 4 a good time? 5 DR. RESTAINO: This is a 6 good time. 7 THE VIDEOGRAPHER: The time 8 is 10:09 a.m., and we are going 9 off the record. 10 (Short break.) 11 THE VIDEOGRAPHER: The time 12 is 10:24 a.m. We are back on the 13 record. 14 BY DR. RESTAINO: 15 Q. Welcome back, Doctor. 16 A. Thank you. 17 Q. When we broke and we were 18 talking about your review of the 19 different epidemiological studies. And I 20 believe you said that your view of this 21 was a bird's-eye-view; is that correct? 22 A. I summarized what I studied 23 from this literature. 24 Q. As far as the strengths and</p>	<p style="text-align: right;">Page 73</p> <p>1 are relevant to my study, but will not be 2 able to comprehensively list all the 3 literatures. 4 Q. How do you determine what is 5 all of the literature? 6 A. You can go to PubMed search 7 or Google Scholar search about the 8 keywords that you have an interest and 9 related to that specific studies. 10 Q. Did you do that before you 11 wrote your expert report in this 12 litigation? 13 A. Yes, I did. 14 Q. And can -- as you sit here 15 today, can you recall and share with us 16 some of the keywords that you used? 17 A. Okay. If I can remember I 18 will let you know, okay. 19 One is talc, talcum powder, 20 ovarian cancer -- could I go slowly -- 21 pathogenesis, tumor initiation, TP53 -- 22 that's a gene name -- high grade serous 23 carcinoma, and of course ovarian cancer. 24 Q. Okay. Do you know the</p>

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<p style="text-align: right;">Page 74</p> <p>1 difference when conducting a review of 2 the literature between a systematic 3 review of the literature and a narrative 4 review of the literature? 5 MS. MILLER: Objection. 6 THE WITNESS: I think that's 7 too general a question, could you 8 become more specific? 9 BY DR. RESTAINO: 10 Q. Yes, sir. Have you heard of 11 the term "systematic review of the 12 literature"? 13 A. The system review of 14 literature is what I did. That's my 15 definition, looked into the search 16 engine, like Google Scholar and PubMed 17 and put in the keywords. Then you will 18 come out with a list of article, right? 19 So then, I scan quickly, the authors, the 20 titles, and to determine whether this is 21 relevant, either by looking at titles and 22 the authors. If I decide it is an 23 interesting one, I will read more 24 carefully.</p>	<p style="text-align: right;">Page 76</p> <p>1 Q. And you were also provided 2 with the report of Dr. Sarah Kane, which 3 you describe in your expert report; is 4 that true, sir? 5 A. I cannot remember that. 6 Q. Do you remember reviewing an 7 expert report of a gynecologic 8 pathologist from up in Boston? 9 A. Oh, yes. 10 Q. Do you recall reviewing the 11 methodology that she used to write her 12 expert report? 13 A. I know she report pathology, 14 methodology, but I need to have the 15 documents before I can further discuss. 16 Q. Okay. Do you know as you 17 sit here today, if she conducted a 18 systematic review of the literature and 19 then wrote her expert report? 20 A. I don't know. 21 Q. Do you know as you sit here 22 today, if you disagree with the 23 methodology that Dr. Sarah Kane utilized 24 to write her expert report?</p>
<p style="text-align: right;">Page 75</p> <p>1 Q. Do you know what is meant by 2 the term "narrative review of the 3 literature"? 4 MS. MILLER: Objection. 5 THE WITNESS: Does that mean 6 review -- read review articles? 7 BY DR. RESTAINO: 8 Q. Yes. 9 A. Okay. That's what you 10 meant? 11 Q. Yes. 12 A. I did that also too 13 occasionally, if this is germane to my 14 study and is useful for the paper. 15 Q. Did you -- and I know it's 16 not a memory test, did you use the 17 keyword "inflammation" when you were 18 doing your search of PubMed, Google 19 Scholar, and whatever database? 20 A. Yes, I believe so. 21 Q. Okay. And you reviewed the 22 expert report of Dr. Sarah Kane, correct? 23 A. I think I was provided with 24 Saed's report.</p>	<p style="text-align: right;">Page 77</p> <p>1 A. I need to see the report 2 first. I cannot recall at this moment. 3 Q. Okay. Do you recall reading 4 Dr. Saed's expert report? 5 A. Yes, I recall it. 6 Q. And you have criticisms of 7 the methodology he employed to write his 8 expert report? 9 A. Yes. And this is in my 10 expert reports shown in Exhibit 2. 11 Q. Yes, sir. Thank you. 12 A. Yeah, here. 13 Q. Now, in -- I believe it's 14 expert -- excuse me -- Exhibit 4, your 15 study report. It's titled "Study Report 16 to Determine Whether Chronic Inflammation 17 Causes Ovarian Cancer." 18 Do you have that, sir? 19 A. Yes. 20 Q. Now, you are the sole author 21 listed on the version that we were 22 provided; is that true? 23 A. Correct. 24 Q. And will there be other</p>

<p style="text-align: right;">Page 78</p> <p>1 authors -- strike that. I'm sorry. 2 Doctor, do you plan on 3 submitting this publication for peer 4 review and publication? 5 A. Yes. 6 Q. Have you submitted it 7 already? 8 A. Not yet. 9 Q. The -- as you sit here 10 today, do you know if the version that 11 you submit for peer review and 12 publication will have co-authors with 13 you? 14 A. I have no plan yet what kind 15 of other data will be included. So I 16 cannot answer the question for the future 17 tense. 18 Q. Is it fair to say then that 19 your study report as provided today is an 20 unfinished product? 21 A. It is an ongoing project. 22 Q. Have you discussed the 23 methodology that you used with this 24 report with any other investigator at</p>	<p style="text-align: right;">Page 80</p> <p>1 the truth from your study, did you 2 discuss the study methodology for 3 example, with Dr. Kurman? 4 MS. MILLER: Objection. You 5 said in discussing how to do the 6 study, but he said he didn't 7 discuss the study. So I'm 8 confused by the question. 9 THE WITNESS: Yeah, I think 10 I answered your question already. 11 BY DR. RESTAINO: 12 Q. Prior to writing your study 13 report, did you discuss what you were 14 doing with Dr. Kurman? 15 A. No. 16 Q. Has Dr. Kurman, to the best 17 of your knowledge, seen the version of 18 the study report that we have at this 19 time? 20 A. I don't know whether he see 21 it or not. 22 Q. Now, if you -- on the first 23 page of your study report, underneath 24 your name and your address, there's time</p>
<p style="text-align: right;">Page 79</p> <p>1 Johns Hopkins University? 2 A. No. 3 Q. Did you study the -- did you 4 discuss the methodology that you would 5 use for your study report with any 6 representative of Johnson & Johnson? 7 A. No. 8 Q. Did you discuss the 9 methodology that you would use for your 10 study report with any scientist that's -- 11 or physician not with Johnson & Johnson 12 and not with Johns Hopkins? 13 A. Could you repeat that 14 question one more time? 15 Q. Did you discuss your 16 methodology with anyone else other than a 17 scientist from Johnson & Johnson or a 18 representative from Johnson & Johnson or 19 physician/scientist from Johns Hopkins? 20 A. As I said, this is my own 21 study. 22 Q. I appreciate that -- that 23 it's your own study. But in discussing 24 how to do the study and how to best glean</p>	<p style="text-align: right;">Page 81</p> <p>1 frame, January 1st, 2019, to February 11, 2 2019; is that correct? 3 A. This time frame was 4 generated based on when I draft this 5 report, and I think I can finish between 6 January 1st to February 11, 2019. That's 7 my projection. 8 Q. In any period of time 9 between January 1st and today, did you 10 share any drafts of your study report 11 with anyone? 12 A. Anyone means? 13 Q. Anyone but you. Has anyone 14 else seen any drafts of your study 15 report? 16 A. I think it's included in 17 this exhibit, so everybody now see it. 18 Q. Okay. Prior to today, and 19 prior to it being distributed amongst the 20 attorneys, did you share any drafts of 21 that report with anyone? 22 A. I did not share it with any 23 of my colleague scientists -- 24 Q. Okay.</p>

<p style="text-align: right;">Page 82</p> <p>1 A. -- and any other colleagues 2 near -- near me. 3 Q. Did you share any draft of 4 the study report with any representative 5 of Johnson & Johnson? 6 A. You mean a draft, no. 7 Q. Okay. Are there drafts of 8 your study report? 9 A. There is no draft. 10 Q. And when you first sat down 11 and thought about what study you would 12 like to do, to look at the question 13 regarding chronic inflammation and 14 ovarian cancer precursor cells, did you 15 write up a protocol for yourself? 16 A. What do you mean protocol? 17 Q. Did you write down a plan 18 for how you anticipated conducting the 19 study? 20 A. No. 21 Q. Now, for your histological 22 analysis, you identified cases that were 23 showing ovarian cancer precursor lesions 24 without concurrent ovarian cancer; is</p>	<p style="text-align: right;">Page 84</p> <p>1 re-reviewed the whole material before I 2 conducted this study and write down my 3 results as shown in the table. 4 Q. So if you wanted to see the 5 slide that had evidence of p53 signature 6 lesions, was there a list of those slides 7 that had that pathology? 8 A. I think that's correct. But 9 I need to re-review -- re-review them. 10 Sometimes they are not present anymore 11 for study because they are very small and 12 minute. 13 Q. I'm sorry, sir, what are 14 small and minute? 15 A. So could you go back to this 16 Figure 2 so I can explain to you what 17 this minute means. 18 Table 2 in my report. 19 Q. The listing of your 59 20 slides? 21 A. No, no, no, not that one. 22 This one. 23 MS. MILLER: He's talking 24 about his report. I think.</p>
<p style="text-align: right;">Page 83</p> <p>1 that correct? 2 A. Yes. But which page are you 3 referring to now? 4 Q. I'm just asking in a general 5 sense. 6 A. Yes. 7 Q. Okay. And then you also 8 selected some cases with ovarian cancer 9 as control; is that correct? 10 A. I -- you must refer to the 11 table, yes. 12 Q. Okay. Now, how did you 13 identify the cases that had ovarian 14 cancer precursor lesions without 15 concurrent ovarian cancer? Were the 16 slides labeled? 17 A. No. It's based on the 18 pathology reports and my re-review of the 19 slides. 20 Q. Who wrote the pathology 21 reports that pertain to each specific 22 slide? 23 A. The individual pathologist 24 who diagnosed that case. And I</p>	<p style="text-align: right;">Page 85</p> <p>1 DR. RESTAINO: Oh, I'm 2 sorry. Forgive me. 3 THE WITNESS: Oh this one 4 here. Page 11 here. 5 BY DR. RESTAINO: 6 Q. Yes, sir. 7 A. So you need to understand 8 this precursor lesions are very small. 9 Q. I understand precursor 10 lesions -- 11 A. Okay. 12 Q. -- probably more than I want 13 to. 14 My question is, sir, if you 15 were going to determine if there were 16 lymphocytes associated or -- or listed in 17 a particular slide with p53 lesions in 18 it, was there a list of the -- of the 19 slides that already had p53 lesions or 20 did you have to go through every slide to 21 find them? 22 A. I think your question has 23 two parts. One is p53 signatures, 24 whether this is listed?</p>

<p style="text-align: right;">Page 86</p> <p>1 Q. Yes.</p> <p>2 A. Okay. I think it is listed.</p> <p>3 But I need to re-review them.</p> <p>4 Q. Okay.</p> <p>5 A. Okay.</p> <p>6 Q. Okay. And then also --</p> <p>7 A. Second question, chronic</p> <p>8 inflammation.</p> <p>9 Q. Okay. Now -- but can the</p> <p>10 same thing be said for the --</p> <p>11 DR. RESTAINO: Excuse me.</p> <p>12 God bless you.</p> <p>13 MS. SHARKO: Thanks.</p> <p>14 BY DR. RESTAINO:</p> <p>15 Q. Regarding other pathology,</p> <p>16 in other words, you looked at the p53</p> <p>17 signature lesions and you also looked at</p> <p>18 the serous tubal intraepithelial cells,</p> <p>19 correct?</p> <p>20 A. Yeah, very good.</p> <p>21 Q. Can we call them STIC?</p> <p>22 A. Please.</p> <p>23 Q. Okay. Did you -- is there a</p> <p>24 listing in the data bank where you</p>	<p style="text-align: right;">Page 88</p> <p>1 look at this slide?</p> <p>2 A. Okay. I get you. So I made</p> <p>3 a diagnosis of p53 signature by myself in</p> <p>4 this study.</p> <p>5 Q. Thank you.</p> <p>6 Okay. So how many slides</p> <p>7 are in the data bank that you --</p> <p>8 A. I don't know. I need to --</p> <p>9 I don't know that number.</p> <p>10 Q. How did you derive or decide</p> <p>11 upon which 59 slides that you were going</p> <p>12 to look at?</p> <p>13 A. I looked at those slides</p> <p>14 with the lesions, and they are available</p> <p>15 for me to review.</p> <p>16 Q. But how did you know which</p> <p>17 slides had which lesions to pull them?</p> <p>18 A. Okay. So your question is,</p> <p>19 how can I select those cases, right?</p> <p>20 Q. Yes, sir.</p> <p>21 A. Okay. So, basically, this</p> <p>22 study we collect all the tubal lesions,</p> <p>23 including p53 signatures and STIC from</p> <p>24 the pool of cases. Then we combine them</p>
<p style="text-align: right;">Page 87</p> <p>1 obtained these slides of the slides with</p> <p>2 STIC lesions in them?</p> <p>3 A. This would be really</p> <p>4 complicated to answer, because basically</p> <p>5 I need to retrieve the slides and I need</p> <p>6 to re-review all of them to make the</p> <p>7 diagnosis. So I will say the diagnosis,</p> <p>8 this -- in this table is based on my</p> <p>9 review of all the cases, is my own</p> <p>10 diagnosis.</p> <p>11 Q. Okay. With that table open</p> <p>12 in front of you, sir, if you took at</p> <p>13 lesion Number 1, the very top one?</p> <p>14 A. Yes.</p> <p>15 Q. Case ID S8001 diagnosis p53</p> <p>16 SIG, does that stand for signature</p> <p>17 lesion?</p> <p>18 A. Yes.</p> <p>19 Q. Okay. Now, did -- did you</p> <p>20 take out slide -- or excuse me, Lesion 1,</p> <p>21 slide S8001, 8001, and did you make the</p> <p>22 diagnosis of p53 signature lesion or was</p> <p>23 there a listing of slides that said, if</p> <p>24 you want to see p53 signature lesion,</p>	<p style="text-align: right;">Page 89</p> <p>1 into our study.</p> <p>2 So in order to know exactly</p> <p>3 is a p53 signature STIC or there is no</p> <p>4 lesion anymore, or there's a cancer, I</p> <p>5 need to review every single case of that.</p> <p>6 Q. So for Slide Number 1, Case</p> <p>7 ID S80001, when you sat down at the</p> <p>8 microscope, you knew that someone had</p> <p>9 already diagnosed p53 signature lesions</p> <p>10 in that slide; is that correct?</p> <p>11 A. I think this cohort -- not</p> <p>12 cohort -- collection, labels, tubal</p> <p>13 lesions, including p53 signature and</p> <p>14 STIC. And sometimes they have STICs and</p> <p>15 p53 signature and cancer or without</p> <p>16 cancer. So it's really complicated.</p> <p>17 It's not only p53 signature.</p> <p>18 This pool that I -- we just</p> <p>19 talking about is the collection of all</p> <p>20 tubal lesions. It's really vague. It's</p> <p>21 just labeled positive. Then I need to</p> <p>22 diagnose and confirm the diagnosis before</p> <p>23 I conduct these experiments.</p> <p>24 Q. Okay. If you would turn to,</p>

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<p style="text-align: right;">Page 90</p> <p>1 in your full study, on Page 1, you have a</p> <p>2 paragraph that you have titled</p> <p>3 "Hypothesis"; is that correct?</p> <p>4 A. Correct.</p> <p>5 Q. And if you look down five</p> <p>6 lines, sir, in the middle of that</p> <p>7 paragraph, towards the right of the</p> <p>8 paragraph, there's a sentence that</p> <p>9 starts, "We hypothesize that if ovarian</p> <p>10 cancer."</p> <p>11 Do you see that, sir?</p> <p>12 A. Oh, okay. Yes.</p> <p>13 Q. If you're the sole author,</p> <p>14 who is the "we"?</p> <p>15 A. Okay. So, let me see this.</p> <p>16 I will actually explain to you. So in</p> <p>17 scientific community, we always use "we."</p> <p>18 So this is engrained into my brain. I</p> <p>19 never say I, because we are not so</p> <p>20 arrogant. Scientists is always very poor</p> <p>21 people.</p> <p>22 MS. MILLER: Sorry to laugh</p> <p>23 at you.</p> <p>24 THE WITNESS: We try to test</p>	<p style="text-align: right;">Page 92</p> <p>1 Carcinoma by elucidating Its Early</p> <p>2 Changes,' Grant Number W81XWH-11-2-0230."</p> <p>3 Did I read that correctly,</p> <p>4 sir?</p> <p>5 A. Yes.</p> <p>6 Q. Now, that's an -- that was</p> <p>7 the ongoing grant that you have many</p> <p>8 publications for; is that correct?</p> <p>9 A. This grant has ended.</p> <p>10 Q. Okay. There's no more money</p> <p>11 to be obtained from that grant?</p> <p>12 A. I wish, but no.</p> <p>13 Q. Now, associated with this</p> <p>14 grant, the slides that were available for</p> <p>15 you to review, are they located at the</p> <p>16 Johns Hopkins University slide bank, or</p> <p>17 did you have to go to another university</p> <p>18 to get them?</p> <p>19 A. It's inside of Johns Hopkins</p> <p>20 research building, and this is a</p> <p>21 government funded, so we are responsible</p> <p>22 to take care of them.</p> <p>23 Q. Okay. And associated with</p> <p>24 each slide, is there a medical history of</p>
<p style="text-align: right;">Page 91</p> <p>1 all the hypothesis, many</p> <p>2 hypothesis, but all failed.</p> <p>3 BY DR. RESTAINO:</p> <p>4 Q. Okay.</p> <p>5 A. So it's really --</p> <p>6 Q. I was just trying to</p> <p>7 confirm, sir, if you did --</p> <p>8 A. Yeah.</p> <p>9 Q. -- this alone or if there</p> <p>10 were others.</p> <p>11 A. Of course. Of course. Of</p> <p>12 course.</p> <p>13 Q. Now, under study design, on</p> <p>14 the next page, you have a paragraph</p> <p>15 titled "Study Design and Case Selection,"</p> <p>16 correct?</p> <p>17 A. Yes.</p> <p>18 Q. And you write, "The cases</p> <p>19 were retrieved from the archival files</p> <p>20 from the ovarian cancer precursor</p> <p>21 registry supported by U.S. Department of</p> <p>22 Defense (USA MPMC) directed medical</p> <p>23 research programs (CDMRP) grant title</p> <p>24 'Prevention of Ovarian High Grade Serous</p>	<p style="text-align: right;">Page 93</p> <p>1 the woman from whom the tissue was</p> <p>2 obtained?</p> <p>3 A. I cannot recall that,</p> <p>4 because it's under the IRB regulations,</p> <p>5 so that's -- I cannot remember correctly</p> <p>6 what IRB said.</p> <p>7 Q. And in fact, in several of</p> <p>8 the publications that you have published</p> <p>9 or co-authored that involves a</p> <p>10 histopathological analysis of the slides</p> <p>11 from this grant that we just discussed,</p> <p>12 you list that you obtained internal</p> <p>13 review board approval, correct?</p> <p>14 A. Correct.</p> <p>15 Q. Did you obtain -- oh, excuse</p> <p>16 me. Internal review board. Would it be</p> <p>17 okay if for the rest of the day, we just</p> <p>18 say IRB?</p> <p>19 A. I agree.</p> <p>20 Q. You're familiar with IRB?</p> <p>21 A. That's why we did study.</p> <p>22 Q. Okay. Did you obtain IRB</p> <p>23 approval to conduct the study that we are</p> <p>24 discussing today?</p>

24 (Pages 90 to 93)

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<p style="text-align: right;">Page 94</p> <p>1 A. I think every time DOD give 2 the fund, they need to approve every 3 regulatory documents. 4 MS. SHARKO: Dr. Shih, he's 5 just asking you, if to do this 6 slide review that you did, you 7 first got IRB approval. 8 THE WITNESS: Yes. And this 9 is required. 10 BY DR. RESTAINO: 11 Q. For this study that we're 12 discussing today, the -- the appropriate 13 IRB gave you approval to do the study? 14 A. Yes. This -- okay. So this 15 study, the IRB in the original form, and 16 actually the IRB continues, okay, even 17 the grant expired, because IRB is defined 18 as the study, not dependent on whether we 19 have it funded or not. It's only 20 research oriented. 21 So we obtain the IRB in the 22 very beginning for many, many years, and 23 so it's include different kinds of 24 studies.</p>	<p style="text-align: right;">Page 96</p> <p>1 Q. You do not -- or do you 2 state in the study report anywhere that 3 IRB approval was obtained? 4 A. Could you repeat the 5 question one more time? 6 Q. Can you show us in the study 7 report that you have in front of you 8 where you state that IRB approval was 9 obtained? 10 MS. MILLER: Objection. 11 Lacks foundation. 12 MS. SHARKO: He wants to 13 know if, looking at your report, 14 you refer anywhere to getting IRB 15 approval. 16 BY DR. RESTAINO: 17 Q. Do you understand what I 18 mean, sir? 19 A. I did not recall I put that 20 in, but in future publication, definitely 21 I will put that in. 22 Q. Okay. In your -- in the 23 version of the study report that we have, 24 can you show me where you discuss the</p>
<p style="text-align: right;">Page 95</p> <p>1 Q. So, is it your testimony 2 that you did not need specific IRB 3 approval to pull these 59 slides and look 4 at them? 5 A. In fact, I submit addendum 6 of the IRB report, including to 7 investigate chronic inflammation in the 8 precursor lesion, and the 9 microenvironment, epigenetic study, and 10 to many other things. 11 Q. And to whom did you submit 12 the addendum? 13 A. To the Johns Hopkins eIRB. 14 Q. And when did you do that? 15 A. I cannot recall. 16 Q. Prior to conducting this 17 study? 18 A. Again, as I said, this study 19 about the chronic inflammation and the 20 microenvironment was ongoing for many 21 years. And as you can see, there's 22 Ardighieri publication, 2014, in the 23 International Journal of GYN Pathology, 24 and this is in continuation.</p>	<p style="text-align: right;">Page 97</p> <p>1 limitations of your study? 2 A. This is the data I want to 3 show to you guys today. But the 4 limitation, definitely I will say that in 5 my publications. And actually in -- I 6 think I put the limitation in more 7 speculated terminology in my study 8 reports, based on my publication records. 9 This is very different from some very 10 sloppy bench science publication, without 11 acknowledge any of the limitation. 12 Q. As you sit here today, do 13 you know if you've ever published a paper 14 pertaining to a study wherein you did not 15 describe the limitations of the study? 16 A. The limitation depends on 17 how you present it. It can become 18 speculative. It is possible. And 19 further study is required. So the 20 limitation, the term may not be used by 21 the implication of the limitations 22 exercise in the report. 23 Q. Do you -- I'm sorry, sir. I 24 did not mean to step on your sentence.</p>

25 (Pages 94 to 97)

<p style="text-align: right;">Page 98</p> <p>1 In the version of the study</p> <p>2 report that was provided to us, can you</p> <p>3 show us where you describe the</p> <p>4 limitations of your study?</p> <p>5 MS. MILLER: Objection. He</p> <p>6 said earlier that --</p> <p>7 THE WITNESS: I did answer</p> <p>8 your question.</p> <p>9 BY DR. RESTAINO:</p> <p>10 Q. Is the word "limitations" to</p> <p>11 be found anywhere in this -- in the</p> <p>12 version of the report that we've been</p> <p>13 provided with?</p> <p>14 A. Again, this is ongoing</p> <p>15 projects, ongoing results, it is by no</p> <p>16 means that this will be the final</p> <p>17 publication report. And of course we</p> <p>18 have not written the paper yet, but when</p> <p>19 we -- when I -- I am sorry. When I</p> <p>20 finish this study and try to publish it</p> <p>21 and when I draft the manuscript,</p> <p>22 definitely like in other publication I</p> <p>23 did, I will use the term to show the</p> <p>24 limitation, but not necessarily using the</p>	<p style="text-align: right;">Page 100</p> <p>1 A. Yes.</p> <p>2 Q. Now, the second sentence</p> <p>3 states, "My recent study, which is</p> <p>4 included in full at the end of this</p> <p>5 report, offers significant support for</p> <p>6 this conclusion."</p> <p>7 Did I read that correctly?</p> <p>8 A. Yes.</p> <p>9 Q. Is it your testimony today</p> <p>10 that the -- your recent study we've been</p> <p>11 discussing is not the full report but is</p> <p>12 going to be modified?</p> <p>13 MS. MILLER: Objection.</p> <p>14 THE WITNESS: This is the</p> <p>15 data I have, but when you wrap up</p> <p>16 a study, you have other</p> <p>17 ingredients, like introduction,</p> <p>18 methodologies, result, discussion.</p> <p>19 This is not full report as a</p> <p>20 publication. I mean a full report</p> <p>21 meaning it's publication. Okay.</p> <p>22 But this is a full result I</p> <p>23 have at this moment.</p> <p>24 BY DR. RESTAINO:</p>
<p style="text-align: right;">Page 99</p> <p>1 term, the word of limitation in the study</p> <p>2 outcome.</p> <p>3 Q. Sir, if you would turn now</p> <p>4 to your expert report instead of the</p> <p>5 study report, but your expert --</p> <p>6 A. Expert report.</p> <p>7 Q. Your expert report, please.</p> <p>8 And -- and turn to Page 16 of your expert</p> <p>9 report.</p> <p>10 Do you see, sir, the first</p> <p>11 full paragraph at the top which starts,</p> <p>12 "In reality," --</p> <p>13 MS. MILLER: Page?</p> <p>14 THE WITNESS: Page 16?</p> <p>15 MS. MILLER: I don't have</p> <p>16 that on Page 16.</p> <p>17 DR. RESTAINO: It may not be</p> <p>18 Page 16.</p> <p>19 Page 15, forgive me.</p> <p>20 BY DR. RESTAINO:</p> <p>21 Q. Page 15. Do you see the</p> <p>22 paragraph up above, it starts, "In</p> <p>23 reality, chronic inflammation."</p> <p>24 Do you see where I am, sir?</p>	<p style="text-align: right;">Page 101</p> <p>1 Q. A moment ago you testified</p> <p>2 that it could change, your opinions could</p> <p>3 change. You state, again, this is</p> <p>4 ongoing projects, ongoing results.</p> <p>5 A. Yes.</p> <p>6 Q. So, is it fair to say that</p> <p>7 your opinions in your expert report, in</p> <p>8 the study report that you've provided to</p> <p>9 us and that you are providing today, are</p> <p>10 preliminary results?</p> <p>11 MS. MILLER: Objection.</p> <p>12 THE WITNESS: Could you</p> <p>13 repeat the question? I think</p> <p>14 there's two questions in your</p> <p>15 previous statement. Could you</p> <p>16 break it up?</p> <p>17 BY DR. RESTAINO:</p> <p>18 Q. You stated that there were</p> <p>19 ongoing results. So if there's ongoing</p> <p>20 results --</p> <p>21 A. No.</p> <p>22 Q. -- is it --</p> <p>23 A. It is ongoing study, not</p> <p>24 results.</p>

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<p style="text-align: right;">Page 102</p> <p>1 Q. Okay. And so that there</p> <p>2 isn't any confusion, particularly on my</p> <p>3 part, sir, I want to give you what's been</p> <p>4 marked as Exhibit 27 I believe.</p> <p>5 (Document marked for</p> <p>6 identification as Exhibit</p> <p>7 Shih-27.)</p> <p>8 BY DR. RESTAINO:</p> <p>9 Q. And do you recognize that</p> <p>10 paper, sir?</p> <p>11 A. Yes, I recognize it.</p> <p>12 Q. Okay. If -- if you turn to</p> <p>13 Page 6546. Okay, sir? Are you there?</p> <p>14 A. Yeah.</p> <p>15 Q. Do you see there's a section</p> <p>16 titled "Acknowledgments"?</p> <p>17 A. Yes.</p> <p>18 Q. And do you see that they --</p> <p>19 that there is written there, "The work</p> <p>20 was supported by the Honorable Tina</p> <p>21 Brozman, B-R-O-Z-M-A-N, Foundation and</p> <p>22 the Department of Defense CDMRP," and</p> <p>23 then there's the grant number that we</p> <p>24 discussed earlier. That's the same grant</p>	<p style="text-align: right;">Page 104</p> <p>1 grant number is listed there, correct?</p> <p>2 A. Correct.</p> <p>3 Q. And that's the same grant</p> <p>4 that we've been talking about so far this</p> <p>5 morning?</p> <p>6 A. This is only one of the</p> <p>7 grants with acknowledgments.</p> <p>8 Q. Okay. And I just wanted --</p> <p>9 for the record, it's the same grant?</p> <p>10 A. Yes.</p> <p>11 Q. Now, for the slides for this</p> <p>12 paper, the methylomic analysis, were they</p> <p>13 obtained from the same Johns Hopkins</p> <p>14 tissue bank?</p> <p>15 A. They are obtained from</p> <p>16 different resources within Johns Hopkins.</p> <p>17 Q. Okay. Now, if you would</p> <p>18 turn to Page 6537 of that article. And</p> <p>19 you'll see there that there is a</p> <p>20 materials and methods section.</p> <p>21 A. Right.</p> <p>22 Q. And the first full sentence</p> <p>23 of that section, it is written, "This</p> <p>24 study was performed after approval by</p>
<p style="text-align: right;">Page 103</p> <p>1 that we have been discussing; is that</p> <p>2 correct?</p> <p>3 A. I think so.</p> <p>4 Q. And were the materials that</p> <p>5 were utilized for this study, "Methylomic</p> <p>6 analysis of ovarian cancers identifies</p> <p>7 tumor-specific alterations readily</p> <p>8 detectable in early precursor lesions,"</p> <p>9 obtained from the same Johns Hopkins</p> <p>10 University tissue or slide bank as your</p> <p>11 present study?</p> <p>12 A. Could you indicate where is</p> <p>13 the sentences?</p> <p>14 Q. I was -- put your attention</p> <p>15 to the acknowledgments. Do you see under</p> <p>16 acknowledgments?</p> <p>17 MS. MILLER: Do you want me</p> <p>18 to show him?</p> <p>19 DR. RESTAINO: Sure. Thank</p> <p>20 you.</p> <p>21 THE WITNESS: Yeah, I saw</p> <p>22 that acknowledgement.</p> <p>23 BY DR. RESTAINO:</p> <p>24 Q. Okay. And you see that the</p>	<p style="text-align: right;">Page 105</p> <p>1 Institutional Review Board (IRB) and</p> <p>2 conducted in accordance with the U.S.</p> <p>3 Common Rule."</p> <p>4 Do you see where I read that</p> <p>5 from, sir?</p> <p>6 A. Yes.</p> <p>7 Q. Will your final paper, your</p> <p>8 study report that when it's submitted for</p> <p>9 publication, will that contain that</p> <p>10 similar language?</p> <p>11 MS. MILLER: Objection.</p> <p>12 THE WITNESS: It will.</p> <p>13 BY DR. RESTAINO:</p> <p>14 Q. But it does not at this</p> <p>15 time, correct?</p> <p>16 A. It's not a paper yet. We</p> <p>17 have not -- I have -- I'm sorry, excuse</p> <p>18 me as a scientist. We are teamwork.</p> <p>19 I did not submit the paper</p> <p>20 yet. I did not write the paper yet.</p> <p>21 Q. So what is it that we are</p> <p>22 looking at when we see the full study</p> <p>23 report, as you describe it, what is that?</p> <p>24 A. Excuse me, what, could you</p>

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<p style="text-align: right;">Page 106</p> <p>1 repeat one more time?</p> <p>2 Q. Exhibit 4, your -- the study</p> <p>3 itself.</p> <p>4 A. Yeah.</p> <p>5 Q. What you describe as being</p> <p>6 attached in full to your expert report,</p> <p>7 if it's not a paper yet, what are we --</p> <p>8 is it, what are we looking at, sir?</p> <p>9 A. It's interim report to show</p> <p>10 that -- to address one of the most</p> <p>11 important questions regarding whether</p> <p>12 talc will cause inflammation,</p> <p>13 inflammation will cause precursor lesion</p> <p>14 where ovarian cancer originate from.</p> <p>15 Q. But your expert report</p> <p>16 describes it as a full report. Is it a</p> <p>17 full report as in your expert report or</p> <p>18 is it an interim report as you just</p> <p>19 stated?</p> <p>20 A. Which were you -- which --</p> <p>21 which one are you talking about? I'm</p> <p>22 confused.</p> <p>23 Q. The study report.</p> <p>24 A. Okay. My study report.</p>	<p style="text-align: right;">Page 108</p> <p>1 consideration."</p> <p>2 Do you have that language in</p> <p>3 the full interim report that you have</p> <p>4 provided to us?</p> <p>5 MS. MILLER: Objection.</p> <p>6 THE WITNESS: I think I</p> <p>7 answered your question already. I</p> <p>8 think in the final publication we</p> <p>9 prepared, I will do that.</p> <p>10 And this is my style. In</p> <p>11 every paper I will be sure this</p> <p>12 will be included.</p> <p>13 BY DR. RESTAINO:</p> <p>14 Q. Thank you, sir. I</p> <p>15 understand.</p> <p>16 As you sit here today, can</p> <p>17 you share with us any of the limitations</p> <p>18 that exist regarding the study you</p> <p>19 conducted that we've been discussing?</p> <p>20 A. Could you repeat one more</p> <p>21 time and more specific, what do you want</p> <p>22 me to do?</p> <p>23 Q. Yes.</p> <p>24 A. Okay.</p>
<p style="text-align: right;">Page 107</p> <p>1 This one?</p> <p>2 Q. Yes.</p> <p>3 A. And where --</p> <p>4 Q. Is that a full report or is</p> <p>5 it an interim report? It's Exhibit 4.</p> <p>6 It should be marked as Exhibit 4.</p> <p>7 A. Yeah, right.</p> <p>8 This is the full report at</p> <p>9 this moment.</p> <p>10 Q. Okay. Going back to the</p> <p>11 paper we just handed to you, the</p> <p>12 methylocmic paper, and if you turn to</p> <p>13 Page 6545.</p> <p>14 Are you there, sir?</p> <p>15 A. Yeah.</p> <p>16 Q. There's a large paragraph,</p> <p>17 right column down towards the bottom that</p> <p>18 starts, "There are a number of</p> <p>19 limitations to our study."</p> <p>20 Do you see that, sir?</p> <p>21 A. Yes.</p> <p>22 Q. Okay. I'll read it in full.</p> <p>23 "There are a number of</p> <p>24 limitations to our study that warrant</p>	<p style="text-align: right;">Page 109</p> <p>1 Q. Thank you, sir.</p> <p>2 What are the limitations of</p> <p>3 your study as you've performed it?</p> <p>4 A. In this Exhibit 4?</p> <p>5 Q. Yes, sir.</p> <p>6 A. Okay. So I think you are</p> <p>7 asking me if I have -- if I wrote or</p> <p>8 write the publication or manuscript,</p> <p>9 including this result, what shall I say,</p> <p>10 right?</p> <p>11 Q. Yes.</p> <p>12 A. So when a scientist write a</p> <p>13 paper -- so for example, I am going to</p> <p>14 write this paper, it depends what kind of</p> <p>15 data I want to include. So this will be</p> <p>16 part of it, and it will join other data,</p> <p>17 which we don't know, to come up with the</p> <p>18 best publication to submit at very high</p> <p>19 impact journal. That's our purpose.</p> <p>20 So at this moment, we don't</p> <p>21 -- I'm sorry, I don't know whether this</p> <p>22 will be a single long paper just</p> <p>23 reporting this finding or in combination</p> <p>24 with other finding as multiple reports or</p>

28 (Pages 106 to 109)

<p style="text-align: right;">Page 110</p> <p>1 a single one publication report. I have 2 no idea yet. 3 Q. But as you sit here today, 4 can you share with us some of the 5 limitations of your study that you as a 6 board-certified pathologist know exists 7 when conducting this study. Do you 8 understand what I'm asking, sir? 9 A. Yes. 10 Q. Okay. What are the 11 limitations to your study as you know 12 them today? 13 A. The other way to put this 14 around is how can I improve this study? 15 Q. No, sir. No, sir. I just 16 want to know, if you were to write today, 17 "The limitations of this study are," what 18 would you write? 19 A. So this is based on the 20 cross-sectioned data at this moment, 21 right? 22 Q. Yes, sir. 23 A. We are not talking about 24 what else would be included?</p>	<p style="text-align: right;">Page 112</p> <p>1 chronic inflammation and the precursor 2 lesions? 3 A. So -- so my opinion as in 4 the Exhibit 2 is not totally dependent on 5 the results. And these results can 6 support some of the important arguments. 7 But again, my opinion will not change, 8 even there is a different result in my 9 official publications. My opinion is 10 based on my literature search about 11 epidemiology, chronic inflammation, 12 carcinogenesis, molecular genetics, and 13 my 20 years of experience as a scientist 14 and pathologist. 15 Q. Sir, if you were to look at 16 another 59 slides, okay, if you were 17 going to -- 18 A. There should be not so many, 19 to be honest. 20 Q. If you were to look at 21 another X number of slides and every one 22 of them shows evidence of chronic 23 inflammation, lymphocytes, macrophages, 24 dendritic cells, all the stuff that we</p>
<p style="text-align: right;">Page 111</p> <p>1 Q. Yes, sir. 2 A. Okay. So I would say I will 3 increase a little bit case number on this 4 because this is from 48 women, 59 5 samples, and this is very important here. 6 This is world's largest study about the 7 precursor lesion without cancer. You 8 cannot ever, ever fund any study with 9 this number, and this is world largest. 10 But we -- as a good 11 scientist like me, I would like to 12 increase the case number a few more to 13 increase the -- to expand more patients. 14 I think that would be important for the 15 reviewers to be highly impressed that we 16 have even more, more than 48 women. 17 Q. Now, in doing so, you will 18 be looking at more slides; is that 19 correct? 20 A. Correct. 21 Q. Okay. And in looking at 22 more slides is it possible that the 23 results will change that will change your 24 opinion regarding the association of</p>	<p style="text-align: right;">Page 113</p> <p>1 learn in pathology and physiology, would 2 that change your opinion regarding the 3 association of chronic inflammation and 4 precursor lesions of ovarian cancer? 5 MS. MILLER: Objection. 6 THE WITNESS: I cannot 7 observe your assumption in the 8 beginning. What you say is 9 looking for this lymphocytes -- 10 you are very good -- NK cells and 11 plasma cells, that's the normal 12 immunity. 13 Every single normal -- your 14 skin, liver, brain, they have 15 those cells. 16 What I'm talking about here 17 is chronic inflammation. Chronic 18 inflammation, of course, contain 19 lymphocytes. But a normal tissue 20 also contain lymphocytes; 21 otherwise, you would get sick, you 22 would get infected, and sepsis. 23 So what I mean chronic 24 inflammation is, as compared to</p>

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<p style="text-align: right;">Page 114</p> <p>1 normal tissue, like I say increase 2 the number and density of those 3 cells. 4 BY DR. RESTAINO: 5 Q. So if you -- 6 A. That's very important. 7 Q. If you were to look at X 8 number of slides -- 9 A. Right. 10 Q. -- and those X number of 11 slides all showed evidence of chronic 12 inflammation associated with the 13 precursor lesions, would your opinion in 14 this regard change? 15 A. I think it's a purely 16 hypothetical. But I can tell you one 17 thing. Based on all scientific practice, 18 when you see zero of 10, then you don't 19 know what's the other two, right. And 20 then if you look at zero -- okay. How 21 about we start over again. 22 We look at two cases and 23 they have no chronic inflammation. So we 24 are not really sure whether this is -- we</p>	<p style="text-align: right;">Page 116</p> <p>1 right? So I think we are pretty safe to 2 reach the conclusion, because we have a 3 really solid basis, zero, of any cases we 4 found. 5 Q. Did you obtain consent from 6 the women from whom these slides came 7 from to evaluate the slides? 8 A. I think I answered that 9 question again, already. 10 We just follow the IRB. 11 What IRB allows to do, we just do it. So 12 I cannot reveal any details, that is 13 privileged and confidential. 14 Q. Would one of the limitations 15 of your study be that you did not have 16 the associated medical records of the 17 women? 18 A. What does that matter? As a 19 scientist, again, the purpose is for the 20 official paper. Again, I don't know what 21 is the title of the official paper is, 22 but the report, as in the Exhibit 4, this 23 table, it is very clearly we try to 24 answer one single question. But in the</p>
<p style="text-align: right;">Page 115</p> <p>1 are really confident about that. 2 But when you look at this 3 number and the -- are you listening? 4 Q. I am listening. I'm reading 5 too. 6 A. So if there is zero of this 7 48 cases, the probability, you know, 8 probability, right, the chances would be 9 extremely, extremely low. 10 So of course I cannot 11 predict what happens. But I think the 12 likelihood that we'll see chronic 13 inflammation in those STIC, p53 14 signature, without cancer, would be very, 15 very low. 16 And especially I would not 17 include another 100, 200 cases, because 18 there's a limitation of the science. 19 There's no such material. 20 Probably I will increase a 21 few number of cases. 22 Even this, in a single one, 23 and this -- use a P-value, 95 percent 24 confidence interval, you know that,</p>	<p style="text-align: right;">Page 117</p> <p>1 paper we may need to answer many 2 questions. 3 But for this specific one, 4 we just want to answer whether -- this is 5 very important -- whether the ovarian 6 cancer precursors, like p53 signature and 7 STIC, has any chronic inflammation. If 8 no, ovarian cancer is not related to 9 chronic inflammation. 10 It could be related to other 11 etiologies, that we, scientist, we are 12 fighting for to look for and to help the 13 women with ovarian cancer. 14 Q. And is it your opinion that 15 the medical history of the women from 16 whom these slides came from is irrelevant 17 for your diagnosis? 18 A. No, definitely not. 19 Q. Then my question -- 20 A. I said -- okay. 21 MS. MILLER: Can you let him 22 finish? 23 THE WITNESS: I have not 24 finished yet.</p>

30 (Pages 114 to 117)

<p style="text-align: right;">Page 118</p> <p>1 What I have said is for this</p> <p>2 particular study -- you can look</p> <p>3 at here -- I want to know whether</p> <p>4 there is increased inflammation</p> <p>5 associated with those precursor</p> <p>6 lesions.</p> <p>7 So in this study, I don't</p> <p>8 need clinical information. But in</p> <p>9 other -- many other ways, other</p> <p>10 studies, we need that information.</p> <p>11 Okay. So it depends on the</p> <p>12 specific question you want to ask.</p> <p>13 You cannot say it's in general</p> <p>14 not. It's not fair.</p> <p>15 BY DR. RESTAINO:</p> <p>16 Q. Are there other limitations,</p> <p>17 other than increasing the case number.</p> <p>18 As you sit here today, can you share with</p> <p>19 us any other limitation of your study?</p> <p>20 A. Limitation to this</p> <p>21 particular question?</p> <p>22 Q. Yes.</p> <p>23 A. Or study I want to publish?</p> <p>24 I'm confused.</p>	<p style="text-align: right;">Page 120</p> <p>1 THE WITNESS: I already</p> <p>2 answer your question.</p> <p>3 For this particular</p> <p>4 questions, I think that's the</p> <p>5 limitation I can think about.</p> <p>6 But for the in the future</p> <p>7 study, because it has not come</p> <p>8 yet, so I don't know what's their</p> <p>9 limitations.</p> <p>10 BY DR. RESTAINO:</p> <p>11 Q. So is it fair to say we</p> <p>12 cannot rely upon this interim study for a</p> <p>13 description of the limitations and how</p> <p>14 those limitations may affect our reading</p> <p>15 of your conclusion?</p> <p>16 A. Already -- okay.</p> <p>17 MS. MILLER: Objection.</p> <p>18 Please, Doctor. Ten seconds.</p> <p>19 THE WITNESS: I have no</p> <p>20 patience.</p> <p>21 MS. MILLER: I know. I'm</p> <p>22 aware. That's very honest of you.</p> <p>23 But please give me a chance. I</p> <p>24 know you're excited to answer the</p>
<p style="text-align: right;">Page 119</p> <p>1 Q. The study report that you</p> <p>2 have in front of us.</p> <p>3 A. Study report. Very good.</p> <p>4 Q. Are there other</p> <p>5 limitations --</p> <p>6 A. Very good.</p> <p>7 Q. -- other than the case</p> <p>8 number and you did not have access to the</p> <p>9 medical records, are there any other</p> <p>10 limitations?</p> <p>11 A. It doesn't mean that I</p> <p>12 cannot access the medical records.</p> <p>13 Q. Did you?</p> <p>14 A. I don't think it's relevant</p> <p>15 to this study.</p> <p>16 Q. Okay. If you would turn now</p> <p>17 to -- yes, thank you.</p> <p>18 A. Which page.</p> <p>19 Q. Other than increasing the</p> <p>20 case number and the -- at this time, not</p> <p>21 review of the medical records, are there</p> <p>22 any other limitations to your study that</p> <p>23 you can share with us?</p> <p>24 MS. MILLER: Objection.</p>	<p style="text-align: right;">Page 121</p> <p>1 question.</p> <p>2 THE WITNESS: I'm very</p> <p>3 excited. Very.</p> <p>4 MS. MILLER: I can see.</p> <p>5 BY DR. RESTAINO:</p> <p>6 Q. Is it fair to say, Doctor,</p> <p>7 that we cannot rely upon this interim</p> <p>8 study for a description of the</p> <p>9 limitations of your study?</p> <p>10 MS. MILLER: Objection.</p> <p>11 THE WITNESS: Yeah, could</p> <p>12 you repeat one more time, slowly</p> <p>13 and using simple language about</p> <p>14 it?</p> <p>15 BY DR. RESTAINO:</p> <p>16 Q. You're -- you're very</p> <p>17 comfortable using English, are you not?</p> <p>18 A. It depends.</p> <p>19 Q. As a matter of fact, you</p> <p>20 quote Shakespeare at times, don't you?</p> <p>21 A. What do you mean that?</p> <p>22 MS. MILLER: Objection.</p> <p>23 BY DR. RESTAINO:</p> <p>24 Q. Do -- you don't know what I</p>

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<p style="text-align: right;">Page 122</p> <p>1 mean by quoting Shakespeare. You know 2 who Shakespeare is? 3 A. I don't think this is my 4 opinion in my report. 5 Q. No, it probably isn't. But 6 have you quoted Shakespeare at lectures? 7 A. I don't know it's me or my 8 co-authors, I cannot remember. 9 Q. I'm asking you. Have you -- 10 MS. MILLER: He said he 11 doesn't remember. 12 BY DR. RESTAINO: 13 Q. -- ever been videotaped 14 wherein you've quoted Shakespeare? 15 A. For what purpose? 16 Q. For educating lay people, 17 perhaps? Have you ever heard of the 18 Endometriosis Foundation? 19 A. Yes. 20 Q. Have you ever -- have you 21 recently been interviewed by them? 22 A. I need to double-check. I 23 never see the interview. 24 Could you show me?</p>	<p style="text-align: right;">Page 124</p> <p>1 "accumulating evidence suggests." 2 Do you see that, sir? It's 3 right about the middle -- as a matter of 4 fact it's right above all the references. 5 There's a sentence that starts 6 "accumulating evidence"? 7 A. Okay. I saw it. 8 Q. And I'll read it and just 9 make sure I read it correctly, sir. 10 "Accumulating evidence suggests that 11 serous tubal intraepithelial" -- 12 "epithelial carcinoma (STIC) or its 13 precursor lesions, including p53 14 signature and serous tubal 15 intraepithelial lesions (STIL) located at 16 fallopian tubes or cortical inclusion 17 cysts of the ovary, are the precursors of 18 ovarian HGSC." And then there's a bunch 19 of references. 20 Did I read that correctly, 21 sir? 22 A. Yes. 23 Q. And that is your opinion 24 today, that these precursor lesions are</p>
<p style="text-align: right;">Page 123</p> <p>1 Q. It's your interview, sir. 2 And you can just look for it on YouTube 3 and -- and on the internet. But you -- 4 you speak English quite well in the 5 interview wherein you quote Shakespeare, 6 is that true? 7 MS. MILLER: Objection. 8 Let's just take down the 9 temperature of it. He is not 10 purporting to not understand 11 things he understands and that's 12 what you're insinuating. 13 DR. RESTAINO: I'm not 14 insinuating anything. I'm saying 15 it. 16 BY DR. RESTAINO: 17 Q. Now, Doctor, let's turn to 18 Page 24 of your study report. The study 19 report. 20 And you see you have a 21 question to ask in the middle, sir? 22 A. Yes. 23 Q. And in the middle of that 24 paragraph, you have language,</p>	<p style="text-align: right;">Page 125</p> <p>1 the precursors of ovarian high grade 2 serous carcinomas; is that correct? 3 A. So are you -- are you asking 4 me about my opinion where is the 5 precursor lesions located? 6 Q. No, sir. I'm just asking, 7 is it your opinion today as you put in 8 your expert report, that the -- that 9 these precursor lesions are the 10 precursors of HGSC? 11 A. That is my opinion, yes. 12 Q. And HGSC, so there's no 13 confusion, is high grade serous 14 carcinoma? 15 A. Perfect. 16 Q. Okay. Thank you. 17 Now, I'd like to hand to you 18 what we have marked as Shih Exhibit 29. 19 (Document marked for 20 identification as Exhibit 21 Shih-29.) 22 BY DR. RESTAINO: 23 Q. And it's an article by 24 Trabert, et al. Have you seen this</p>

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<p>1 article before, sir?</p> <p>2 A. May I have the time to see</p> <p>3 the content in order to recall my memory,</p> <p>4 okay. Just a few -- give me a few</p> <p>5 seconds.</p> <p>6 I don't recall this paper.</p> <p>7 Q. You don't. Do you recall</p> <p>8 writing an editorial about this paper?</p> <p>9 A. Well, maybe. I need to</p> <p>10 see -- make sure that I -- this bringing</p> <p>11 to my memory first.</p> <p>12 Q. As you sit here today, do</p> <p>13 you recall writing and publishing that</p> <p>14 this was an important study for which the</p> <p>15 authors should be congratulated? Does</p> <p>16 that sound familiar?</p> <p>17 A. I cannot recall the</p> <p>18 sentence. You have it -- can you show</p> <p>19 me, please?</p> <p>20 Q. I just want to know if you</p> <p>21 recall saying that. The literature will</p> <p>22 show what the literature shows.</p> <p>23 If you would turn to</p> <p>24 Page 755 of this paper. And are you</p>	<p>1 Q. Did I read that correctly,</p> <p>2 sir?</p> <p>3 A. Yes. This is the word in</p> <p>4 the paper. But it may not --</p> <p>5 Q. Okay. Can you tell us what</p> <p>6 is meant by the word carcinomatosis?</p> <p>7 A. This is a term that medical</p> <p>8 doctors and scientists used to the</p> <p>9 spread -- the spread of ovarian cancer,</p> <p>10 in peritoneal cavity or elsewhere.</p> <p>11 Q. Does carcinomatosis only</p> <p>12 apply to ovarian cancer?</p> <p>13 A. No.</p> <p>14 Q. Now, what they write here is</p> <p>15 that the STIC lesions can be found as</p> <p>16 little as in 11 percent of cases when the</p> <p>17 tube is extensively scrutinized; is that</p> <p>18 correct?</p> <p>19 A. But this is referred to</p> <p>20 Reference 13. It's not --</p> <p>21 That's for me?</p> <p>22 MS. MILLER: Yes.</p> <p>23 THE WITNESS: Okay. Thank</p> <p>24 you. I'm sorry.</p>
Page 127	Page 129
<p>1 there, sir?</p> <p>2 A. Let me see.</p> <p>3 Okay. In Table 3 you meant?</p> <p>4 Q. No. Just on Page 755, if</p> <p>5 you look in the right column, all the way</p> <p>6 down, that little paragraph that starts</p> <p>7 and goes over to the next page.</p> <p>8 Do you see that, sir?</p> <p>9 A. Starting for "STIC is</p> <p>10 found"?</p> <p>11 Q. Perfect.</p> <p>12 A. Okay.</p> <p>13 Q. "STIC is found with</p> <p>14 late-stage high-grade serous carcinomas</p> <p>15 in 11 percent to 61 percent of cases when</p> <p>16 the tube is extensively scrutinized;</p> <p>17 however, limited molecular data suggest</p> <p>18 that STIC is not always the source of</p> <p>19 carcinomatosis. Reference Number 13."</p> <p>20 Did I read that correctly?</p> <p>21 A. 13, let me see which</p> <p>22 reference. Is Chan, by Chan, et al.</p> <p>23 STIC associated with high grade serous</p> <p>24 carcinoma, systemic review. 2017. Okay.</p>	<p>1 BY DR. RESTAINO:</p> <p>2 Q. Do you agree that that's</p> <p>3 what the statement says, that STIC is</p> <p>4 found with late-stage high-grade serous</p> <p>5 carcinomas in 11 to 61 percent of cases?</p> <p>6 That was what is written in</p> <p>7 a study that I represent to you, you</p> <p>8 describe as an important study for which</p> <p>9 the authors should be congratulated?</p> <p>10 A. No. This is for the</p> <p>11 Reference 13, okay? So it's not this</p> <p>12 paper. It's a Reference 13. So you need</p> <p>13 to go back to original paper by Chan, et</p> <p>14 al.</p> <p>15 Do you have the paper so we</p> <p>16 can discuss it further?</p> <p>17 Q. Is it your knowledge as you</p> <p>18 sit here today, that STIC is found with</p> <p>19 late stage high grade serous carcinomas</p> <p>20 in 11 to 61 percent of cases when the</p> <p>21 tube is extensively scrutinized?</p> <p>22 MS. MILLER: Objection.</p> <p>23 THE WITNESS: So could you</p> <p>24 repeat your question and what do</p>

<p style="text-align: right;">Page 130</p> <p>1 you -- what is your specific 2 question that you want me to 3 answer? 4 BY DR. RESTAINO: 5 Q. Is it your -- 6 A. And your question about 7 Number 13, then we need to review the 8 article. We can discuss. I'm happy to 9 do that. 10 Q. I want to discuss what was 11 published by Trabert, et al., last year, 12 in a study you described as an important 13 study for which the authors should be 14 congratulated. 15 Is it your expert opinion 16 that STIC lesions are found with late 17 stage high grade serous carcinomas 18 between 11 and 61 percent of the time? 19 MS. MILLER: Objection. 20 Multiple objections to this 21 question. You are refusing to 22 show him where he made this 23 statement. It's completely taken 24 out of context. We don't -- I</p>	<p style="text-align: right;">Page 132</p> <p>1 tumors, but also suggested that 2 25 percent (2 in 8) of STICs were 3 metastases from other organ sites, (e.g., 4 endometrium)." And Reference 31. 5 "If corroborated these data 6 challenge the view that identification of 7 STIC automatically justifies labeling a 8 concurrent cancer as a tubal primary." 9 Did I read that correctly? 10 A. This has been written in the 11 paper, in the discussion. It's not the 12 author's results. So don't get confused 13 about their discussion and their data. 14 Okay. 15 So this is in a discussion. 16 And also you see the 31, the 17 Reference 31. So it's by Eckert, 18 published in 2016, Cancer Discovery. 19 So could you please show me 20 the Cancer Discovery paper, and I can 21 show you what's going on. 22 Q. Doctor, as you sit here 23 today, do you recall any paper describing 24 genomic analysis revealing STICs as</p>
<p style="text-align: right;">Page 131</p> <p>1 think you should show him his 2 editorial to be fair. 3 THE WITNESS: Number 13. 4 MS. MILLER: And he's saying 5 that he cannot respond to this 6 question without seeing the 7 underlying study that it cites. 8 And you are asking him if he 9 agrees with it, and he's saying he 10 wants to see the study to know if 11 he agrees with it. 12 THE WITNESS: Yes. 13 MS. MILLER: I think those 14 are reasonable points that he's 15 making. 16 BY DR. RESTAINO: 17 Q. Okay. Let's move on then to 18 the top of Page 756. 19 Very first sentence on the 20 next page, sir. Top of Page 756. They 21 write, Trabert, et al., writes, "A recent 22 genomic analysis revealed STIC as a 23 precursor of sporadic high grade serous 24 carcinoma in 50 percent (4 in 8) of</p>	<p style="text-align: right;">Page 133</p> <p>1 precursors of sporadic high grade serous 2 carcinoma in 50 percent of tumors and 3 also suggested 25 percent were mets from 4 other organ sites. 5 Do you recall that? 6 MS. MILLER: Objection. 7 THE WITNESS: You need to 8 show me the documents before 9 further discussion. 10 BY DR. RESTAINO: 11 Q. While we're looking for that 12 and pulling it to show you, can you 13 explain to the court, what are 14 metastases? What is meant by the word 15 "metastases" as it relates to cancer? 16 A. Sure. That's my pleasure. 17 So metastasis is a term that is broadly 18 used by cancer biologist, cancer 19 geneticist, and also pathologist. For 20 me, and many people will agree, that 21 metastasis is an additive -- is an 22 additive process that the tumor cells in 23 their primary location need to break 24 their basement membrane and go into the</p>

<p style="text-align: right;">Page 134</p> <p>1 stroma, S-T-R-O-M-A, stroma tissue, and 2 to find the lymphatic or blood vessel and 3 go into there and circulate. 4 Then -- and it's only 5 50 percent, then circulate, because you 6 are asking me about metastasis. 7 Q. I just asked you the 8 definition of metastasis. Would you 9 agree that a metastasis is the spread of 10 cancer from a primary tumor to a distant 11 site? 12 MS. MILLER: Objection. 13 BY DR. RESTAINO: 14 Q. Simple as that. Would you 15 agree that's what is meant by metastasis 16 in cancer research? 17 MS. MILLER: Objection. 18 THE WITNESS: It depends on 19 who you are asking. For me, okay, 20 you want to ask me my opinion -- 21 BY DR. RESTAINO: 22 Q. Do you disagree with that 23 definition? 24 A. No, I did not say that.</p>	<p style="text-align: right;">Page 136</p> <p>1 cancer biologist see the word 2 "metastases" there, does that suggest to 3 you that the cells they observed came 4 from somewhere else and were not the 5 primary lesion? 6 A. You can say that. 7 Q. Okay. Now if you can turn 8 to what we gave to you as the Eckert 9 paper. 10 (Document marked for 11 identification as Exhibit 12 Shih-30.) 13 BY DR. RESTAINO: 14 Q. That was their Reference 31. 15 Do you recognize this paper, sir? 16 A. I remember seeing this 17 paper. But I cannot recall in detail. 18 So I need to -- 19 Q. Let's read the first couple 20 sentences of the abstract. "Accumulating 21 evidence has supported the fallopian tube 22 rather than the ovary as the origin for 23 high grade serous ovarian cancer, 24 (HGSOC). To understand the relationship</p>
<p style="text-align: right;">Page 135</p> <p>1 Okay, as I said, my opinion, metastasis 2 is an additive process that need to leave 3 the primary site, go into broad 4 circulation and settle down in the other 5 place. 6 Q. So if there are metastatic 7 lesions in the fallopian tube, then by 8 definition, those metastatic cells have 9 come from somewhere else, correct? 10 MS. MILLER: Objection. 11 THE WITNESS: I would say 12 disseminated, not metastasis. So 13 this is quite confusing, even in 14 pathology field. 15 BY DR. RESTAINO: 16 Q. Well, if we go to the 17 Trabert study. 18 A. Trabert. Okay. 19 Q. Okay. And 756, these 20 researchers state that -- they use the 21 word "metastases." They do not use the 22 word "disseminated." Would you agree? 23 A. It was written that way. 24 Q. Okay. So when you as a</p>	<p style="text-align: right;">Page 137</p> <p>1 between putative precursor lesions and 2 metastatic tumors, we performed 3 whole-exome" -- E-X-O-M-E -- "sequencing 4 on specimens from eight HGSOC patient 5 progression series consisting of serous 6 tubal intraepithelial carcinomas (STIC), 7 invasive fallopian tube lesions, invasive 8 ovarian lesions, and omental metastases." 9 Did I read that correctly, 10 sir? 11 A. It was written this way. 12 Q. Okay. Thank you. And 13 putative precursor lesions means 14 reported, or reputed to be precursor 15 lesions, correct? 16 A. I get lost. Let me see. 17 Which line are you at right now? I'm 18 sorry. Which line? 19 Q. One, two, three lines down. 20 A. Three down. Okay. 21 Q. Underneath accumulating 22 evidence, they describe them as putative 23 precursor lesions. 24 Do you see that?</p>

<p style="text-align: right;">Page 138</p> <p>1 A. "Phylogentic analyses 2 supported STIC as a precursor." That's 3 what you are talking about, or before 4 that? 5 Q. Just the third line, sir. 6 A. From the top? 7 MS. MILLER: "To understand 8 the relationship"? 9 DR. RESTAINO: Right next -- 10 pardon me? 11 MS. MILLER: Are you at "To 12 understand the relationship"? 13 BY DR. RESTAINO: 14 Q. Forgive me. Yes. "To 15 understand the relationship between 16 putative precursor lesions," do you see 17 where I am? 18 A. Okay. 19 Q. Okay. Now, stop at the word 20 "putative." 21 Do you see that? 22 A. That's the author's opinion. 23 Q. In this peer-reviewed 24 published paper, correct?</p>	<p style="text-align: right;">Page 140</p> <p>1 expert report. You don't state they are 2 putative. You say they are precursor 3 lesions, correct? 4 A. This is based on -- there 5 are many hypotheses -- 6 MS. MILLER: He's in the 7 middle of answering a question. 8 DR. RESTAINO: I know. I'm 9 just asking if you are ready for a 10 break. 11 THE WITNESS: So I -- 12 DR. RESTAINO: I'm sorry. I 13 misunderstood what you were 14 asking, or what you were -- my -- 15 my -- I misread your body 16 language. And I was -- I thought 17 I was answering you. I'm sorry. 18 MS. MILLER: No, no, no. 19 Wait. 20 BY DR. RESTAINO: 21 Q. Forgive me, sir. 22 A. Could you repeat one more 23 time your question? 24 Q. Yes. These authors describe</p>
<p style="text-align: right;">Page 139</p> <p>1 A. This is not peer-reviewed. 2 I'm sorry. This is a true original 3 publication. I think you get confused. 4 Q. You don't believe that this 5 paper by Eckert, et al., that has been 6 published in Cancer Discovery is 7 peer-reviewed? 8 A. It's -- it's peer-reviewed, 9 but it's not review paper. Maybe we got 10 lost from -- 11 Q. Well, we know it's not a 12 review paper. But it's been reviewed by 13 peers of these authors. Would you agree? 14 A. That's correct. 15 Q. Okay. And they allowed the 16 use "putative precursor lesion," correct, 17 because that's why it's in the article? 18 A. In science we just use a 19 more liberal way to describe things, 20 because we are not very sure about 21 things. 22 Q. Well, you're sure that these 23 lesions are precursors to high grade 24 serous carcinoma, as you write in your</p>	<p style="text-align: right;">Page 141</p> <p>1 the lesions as putative precursor 2 lesions. You state in your expert report 3 that they are precursor lesions. Do you 4 disagree with these authors? 5 A. In order to answer your 6 question, I need to give you background 7 about the -- this field. Because this is 8 a medicine field -- 9 Q. I don't need background on 10 it, trust me on this, sir, I don't need 11 background on it. I just need to know 12 whether it's your opinion that the STIC 13 lesions and the p53 signature lesions are 14 putative precursor lesions, or if they 15 are precursor lesions. 16 A. I would say they are most 17 biologically plausible precursors at this 18 moment. 19 Q. Okay. At this moment. But 20 it might change, because research never 21 finishes, correct? 22 A. But we are talking about the 23 science here as you elaborate in the very 24 beginning.</p>

<p style="text-align: right;">Page 142</p> <p>1 Q. Okay. Now, if you go down 2 to Page 1348 of the Eckert study. Are 3 you there, sir? 4 A. Yes. 5 Q. And it's the first full 6 paragraph in the right column. 7 A. First. 8 Q. Okay. The first full 9 paragraph starts with "the data presented 10 herein." 11 Do you see that, sir? 12 A. Yes. 13 Q. "The data presented herein 14 may lead us to develop our perception of 15 STIC further: STIC in HGSOC could be 16 primary or metastatic." 17 Do you agree with that, sir? 18 A. No. 19 Q. You disagree with these 20 authors that it could be a primary, or it 21 could be metastatic? 22 A. I disagree about the 23 statement. 24 Q. Okay. Sir, did you, in your</p>	<p style="text-align: right;">Page 144</p> <p>1 the first paragraph of the expert. 2 There's a sentence that starts with 3 "phylogenetic analyses." 4 Do you see that, sir? 5 A. No. 6 Q. It's about four or five 7 lines up from the bottom of the first 8 paragraph. 9 A. Ah, the first paragraph. 10 Okay. One, two, three, four, five. 11 Phylogenetic analysis... 12 Q. Do you want to read that 13 into the record out loud, sir, or you 14 want me to? 15 A. You do it. You do a better 16 job. 17 Q. Phylogenetic -- I don't know. 18 Phylogenetic -- 19 MS. MILLER: Slowly. 20 THE WITNESS: I'm not 21 English speaking. 22 BY DR. RESTAINO: 23 Q. You know, English is my 24 second language and I don't have a first.</p>
<p style="text-align: right;">Page 143</p> <p>1 study for which we have your interim 2 report, did you conduct phylogenetic 3 analyses of the material? 4 A. Could you repeat that 5 question one more time? 6 Q. In the slides, the materials 7 you reviewed for the study report we're 8 discussing, did you conduct phylogenetic 9 analysis? 10 A. The study that's in 11 Exhibit 4, as I said many times, the 12 purpose is to determine whether there is 13 a chronic inflammation associated with 14 those precursor lesions. So what is 15 phylogenetic coming to this picture? I 16 cannot understand your question. It's 17 not relevant. 18 Q. Okay. Sir, if you would go 19 back to the abstract of the Eckert paper 20 that we're looking at. 21 A. Okay. 22 Q. Okay. And now to make it a 23 little easier, it's one, two, three, 24 four, five lines up from the bottom of</p>	<p style="text-align: right;">Page 145</p> <p>1 "Phylogenetic analyses 2 supported STIC as precursor lesions in 3 half of our patient cohort, but also 4 identified STIC as metastases in two 5 patients." 6 Did I read that correctly, 7 sir? 8 A. That has been written this 9 way. 10 Q. Okay. So now my question 11 is, did you conduct a phylogenetic analysis 12 of the tissue that you examined for your 13 study report? 14 A. Again, my study report is 15 not answer this question whether the STIC 16 is a precursor or not. I think it has 17 been shown in many papers. 18 The question is, what I want 19 to show is, whether there is chronic 20 inflammation associated with the 21 precursor. I think that is most 22 important question. Whether chronic 23 inflammation has ever, ever played a role 24 in this tumor initiation.</p>

<p style="text-align: right;">Page 146</p> <p>1 I hope you agree that this</p> <p>2 is the best study to show in this way,</p> <p>3 rather than a genetic tree, because it is</p> <p>4 not relevant. We are answering different</p> <p>5 questions.</p> <p>6 Q. Okay. But in order to</p> <p>7 answer the question that you seek to --</p> <p>8 to answer, as Trabert stated in</p> <p>9 referencing --</p> <p>10 A. Trabert?</p> <p>11 Q. The Trabert study.</p> <p>12 A. Yeah.</p> <p>13 Q. They referenced, remember,</p> <p>14 Number 31, on Page 756, in the right</p> <p>15 column. And they referenced the Eckert</p> <p>16 study showing that 25 percent of the</p> <p>17 tumors that are --</p> <p>18 A. Tumors, are you talking STIC</p> <p>19 or carcinoma?</p> <p>20 Q. -- that 25 percent of the</p> <p>21 STICs were metastasis from other organ</p> <p>22 sites, correct?</p> <p>23 A. That has been written.</p> <p>24 Q. Okay. Now, it is your</p>	<p style="text-align: right;">Page 148</p> <p>1 want clarity.</p> <p>2 BY DR. RESTAINO:</p> <p>3 Q. Of those 59 slides as you</p> <p>4 sit here today, how many -- what</p> <p>5 percentage of the STIC lesions developed</p> <p>6 there at the primary site that you</p> <p>7 examined or were metastases from</p> <p>8 elsewhere?</p> <p>9 MS. MILLER: Objection.</p> <p>10 THE WITNESS: You ask very</p> <p>11 important question. I think the</p> <p>12 methodology matters a lot in this</p> <p>13 field.</p> <p>14 So many study in the past,</p> <p>15 they analyze, can I show you the</p> <p>16 Figure 2? I think it will be much</p> <p>17 easier to explain it to you. Or</p> <p>18 you don't need it? I think it</p> <p>19 will be useful for you.</p> <p>20 BY DR. RESTAINO:</p> <p>21 Q. Oh the diagram. The</p> <p>22 cartoon?</p> <p>23 A. The cartoon, yeah. Right.</p> <p>24 Q. Sir it's a simple question.</p>
<p style="text-align: right;">Page 147</p> <p>1 hypothesis, that chronic inflammation was</p> <p>2 not seen in the STIC lesions and the p53</p> <p>3 signature lesion slides that you</p> <p>4 observed, correct?</p> <p>5 MS. MILLER: Objection.</p> <p>6 THE WITNESS: I think I</p> <p>7 already tell you about the answer.</p> <p>8 BY DR. RESTAINO:</p> <p>9 Q. Of the slides that you saw?</p> <p>10 A. Which slides are you talking</p> <p>11 about?</p> <p>12 Q. The 59 slides that make up</p> <p>13 your expert report, sir.</p> <p>14 MS. MILLER: Objection.</p> <p>15 They do not make up his expert</p> <p>16 report.</p> <p>17 DR. RESTAINO: Of the study</p> <p>18 report.</p> <p>19 BY DR. RESTAINO:</p> <p>20 Q. The 59 slides that are</p> <p>21 listed in your study report.</p> <p>22 DR. RESTAINO: Thank you,</p> <p>23 Jessica.</p> <p>24 MS. MILLER: Sorry. I just</p>	<p style="text-align: right;">Page 149</p> <p>1 What percentage of the STICs</p> <p>2 lesions that you evaluated were</p> <p>3 metastases?</p> <p>4 A. Do you remember, when you</p> <p>5 read my study report carefully, I say --</p> <p>6 this is very important. I think this is</p> <p>7 a whole confusing point for your part.</p> <p>8 I say in order to prevent</p> <p>9 this metastases, I intentionally focus on</p> <p>10 studying those STIC and precursor</p> <p>11 signature with cancer, so they cannot</p> <p>12 metastases.</p> <p>13 Q. Were there STIC lesions in</p> <p>14 women who had concurrent ovarian cancer?</p> <p>15 A. I include those as well.</p> <p>16 Q. And what percentage of those</p> <p>17 STIC lesions were metastases?</p> <p>18 A. There are very few. So it's</p> <p>19 not the purpose of this study report.</p> <p>20 The study report, again, is not for that</p> <p>21 purpose.</p> <p>22 Q. Would -- would you agree</p> <p>23 that if sub -- that if X number of the</p> <p>24 STIC lesions you evaluated were</p>

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<p>1 metastases, then the absence of chronic 2 inflammation around that STIC lesion, as 3 you're looking at it, might not exist 4 because the chronic inflammation is back 5 at the primary tumor, wouldn't you agree? 6 A. I think this is too long 7 question. Could you break up small one, 8 and simple one individually so I can 9 better answer you and more effectively. 10 Q. If chronic inflammation 11 caused cancer somewhere, and that -- 12 A. If. Okay. In ovarian 13 cancer or in other tissue types? 14 Q. In an anatomic site where 15 metastases could go to the fallopian 16 tube. And that tumor spread or 17 metastasized to the fallopian tube and 18 was on some of the slides that you looked 19 at that were labeled STIC, you wouldn't 20 expect to see chronic inflammation around 21 those lesions as the precursor to their 22 development, would you? 23 MS. MILLER: Objection. 24 THE WITNESS: I think you're</p>	<p>1 But I guess you only -- do you 2 want to come back and do a half an 3 hour and then go to lunch? It's 4 kind of early. 5 DR. RESTAINO: Does that 6 work for everyone? 7 MS. MILLER: Yes. 8 DR. RESTAINO: I just need 9 to -- 10 THE VIDEOGRAPHER: The time 11 is 11:44 a.m. We're going off the 12 record. 13 (Short break.) 14 THE VIDEOGRAPHER: The time 15 is 12:03 p.m. We are back on the 16 record. 17 BY DR. RESTAINO: 18 Q. Welcome back, Dr. Shih. 19 A. Can I have one small comment 20 here? Or no? There's some confusion 21 about the terminology we just discussed 22 about the STIC. 23 Q. Sir, I don't have a question 24 pending. What I should have shared with</p>
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<p>1 asking whether the STIC with and 2 without cancer, they are 3 associated with chronic 4 inflammation; is that correct? 5 BY DR. RESTAINO: 6 Q. I was asking about the STICs 7 that were present in the slides from 8 women who had a concurrent ovarian 9 cancer. 10 A. Yes. 11 Q. Were those STIC cells 12 primary there at the site that you 13 examined, or were they metastases or 14 don't you know? 15 A. That, I don't know. 16 DR. RESTAINO: The water is 17 having its effect on me. May we 18 take a break? 19 THE WITNESS: I think that's 20 a good idea. 21 THE VIDEOGRAPHER: The time 22 is 11:43 -- 23 MS. MILLER: It's 11:43. I 24 was going to try to go till lunch.</p>	<p>1 you in the beginning of the deposition, 2 and I forgot to do so. There are times 3 when I might ask you a question that I'm 4 asking, just yes or no, but you want to 5 explain it further. 6 At the end of the deposition 7 today, Jessica gets to then also ask you 8 questions. 9 "Now, do you remember when 10 John asked you this question? Would you 11 like to expand upon it?" 12 So if you're cut off, you're 13 not totally cut off. You'll get a chance 14 to explain it. 15 I would like for you to go 16 to your expert report. And if you look 17 on Page 10 of the expert report, you have 18 a table there, correct? 19 A. Right. 20 Q. And then under the table 21 that's a paragraph that's listed, or has 22 a designation of Number 1, correct? 23 MS. MILLER: "The new 24 paradigm"</p>

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<p style="text-align: right;">Page 154</p> <p>1 BY DR. RESTAINO: 2 Q. Yes. The new paradigm. 3 A. The new paradigm. 4 Q. Yes. "The new paradigm of 5 ovarian cancer genesis -- that ovarian 6 serous carcinomas originate not in 7 ovarian tissues, but rather in the 8 precursor lesions in the fallopian 9 tubes -- has been widely accepted (Kurman 10 and Shih Ie, 2011, 2016; Kurman and Shih, 11 2010; Wu, et al., 2018)." 12 Did I read that correctly, 13 sir? 14 A. Yes. 15 Q. Now, the first article, 16 Kurman and Shih Ie, 2011, that's you; is 17 that correct? 18 A. Correct. 19 Q. And Dr. Kurman, that is 20 Dr. Robert Kurman? 21 A. Correct. 22 Q. And did you train under 23 Dr. Kurman? 24 A. I worked with him, yes.</p>	<p style="text-align: right;">Page 156</p> <p>1 A. Correct. 2 Q. Doctor, is it -- so for 3 support of your opinion that the ovarian 4 serous carcinomas originated not in 5 ovarian tissues, but rather in the 6 precursor lesions in the fallopian tube 7 has been widely accepted, the only papers 8 that you have listed to support that 9 statement are statements -- are papers 10 which you and Dr. Kurman are the authors, 11 correct? 12 A. No. 13 Q. Is there another paper there 14 that is not -- where you and Dr. Kurman 15 are not an author? 16 A. So if you -- 17 Q. Sorry, Doctor. Is there 18 another paper listed in your expert 19 report that does not list Dr. Kurman or 20 you as the author? 21 MS. MILLER: Objection. 22 THE WITNESS: There are so 23 many paper. These are review 24 papers based on many, many</p>
<p style="text-align: right;">Page 155</p> <p>1 Q. Okay. Is Dr. Kurman an 2 expert for Johnson & Johnson in this 3 litigation also? 4 A. That's my understanding. 5 Q. Okay. Now, the next one is 6 Kurman and Shih Ie, 2016, correct? 7 A. Correct. 8 Q. And that, again, Dr. Shih is 9 you, correct? 10 A. Correct. 11 Q. The next one is Kurman and 12 Shih 2010. And that's the same 13 Dr. Robert Kurman and the same Dr. Shih, 14 correct? 15 A. Correct. 16 Q. And then the final article 17 is Wu, et al., 2018, correct? 18 A. Correct. 19 Q. And you are actually an 20 author with Dr. Wu; is that correct? 21 A. I'm the co-author. 22 Q. You're a co-author with 23 Dr. Wu. In fact -- yes, that's the 24 genomic landscape paper, correct?</p>	<p style="text-align: right;">Page 157</p> <p>1 reviews. 2 So if you go to references 3 of this paper, you will be readily 4 identifying there's many other 5 articles. 6 But because we don't need to 7 show everyone here, because, you 8 know, based on my status and 9 Dr. Kurman's expertise in this 10 field, we are well recognized as 11 the paradigm shifter along with 12 other investigators in the 13 nations. So I don't think this is 14 a question here. 15 BY DR. RESTAINO: 16 Q. Okay. Sir, in your expert 17 report that you've submitted to the 18 court, would you agree that the only 19 articles that you've referenced for 20 support of your opinion that this 21 hypothesis has been widely accepted are 22 papers that you and Dr. Kurman are 23 co-authors on, correct? 24 A. Again, they are review</p>

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<p style="text-align: right;">Page 158</p> <p>1 papers based on many, many original 2 studies. 3 DR. RESTAINO: I'm going to 4 move to strike. 5 BY DR. RESTAINO: 6 Q. The only papers listed in 7 your expert report are those that you and 8 Dr. Kurman are the co-authors on, 9 correct? 10 A. They are review papers -- 11 MS. MILLER: Objection. 12 Please remember to give me 13 ten seconds. 14 THE WITNESS: I'm sorry. 15 BY DR. RESTAINO: 16 Q. Do you agree with that 17 statement, sir? 18 A. They are review papers based 19 on many original articles. 20 Q. Review papers for which you 21 and Dr. Kurman are the co-author, 22 correct? 23 A. Our review paper is summary 24 of all many original articles.</p>	<p style="text-align: right;">Page 160</p> <p>1 labeled. 2 Q. Okay. So -- 3 A. And assigned. 4 Q. So if you pick up 5 Slide S8001, it already has that number 6 on it? 7 A. I think it should be written 8 on the slides. 9 Q. You think, sir, or you know 10 that they are? 11 A. As I recall they should be 12 there. 13 Q. And the next column has a 14 diagnosis of p53 SIG. Could we agree 15 that SIG stands for signature lesion? 16 A. Yes. 17 Q. And on that slide, S8001, 18 does it list p53 SIG on it? 19 A. You mean on the slides? 20 I -- 21 Q. Is it listed somewhere, so 22 that if you pick up this slide, S8001, 23 you're able to look and say ah, p53 24 signature lesions?</p>
<p style="text-align: right;">Page 159</p> <p>1 Q. Okay. If you would go now 2 down to your study report, which I think 3 is Exhibit 4. 4 A. Yes. 5 Q. And go to Page 26. 6 Actually, I think it's the bottom of 25. 7 It's where your Table 2 is the listing of 8 the slides. 9 MS. MILLER: There's nothing 10 on the table on Page 25. I'm 11 confused. Are you looking for 12 this, on Page 29? 13 DR. RESTAINO: Yes. 29. 14 Thank you. 15 BY DR. RESTAINO: 16 Q. 29. Who drew up this table, 17 sir? 18 A. Repeat the question one more 19 time. 20 Q. Who made up this table? 21 A. I did. 22 Q. Okay. Who named Lesion 1 -- 23 who gave it a case ID of S8001? 24 A. This is from the slides</p>	<p style="text-align: right;">Page 161</p> <p>1 A. Based on this Table 2. 2 Q. Yes. 3 A. Yes. Based on this Table 2. 4 Q. Okay. And this slide did 5 not have evidence of concurrent cancer, 6 correct? 7 A. Yes. 8 Q. At the bottom of Table 2, 9 you define, where the asterisk is, 10 inflammation and you define it as, 11 "Increased lymphocytic infiltrate 12 associated with the lesions as compared 13 to the background normal tissue of 14 mucosa"; is that correct, sir? 15 A. Yes. 16 Q. And that's the definition 17 you used in the entire chart for whether 18 there was inflammation or not? 19 A. As I believe I also look at 20 this plicae fusion, P-L-I-C-A-E, fusion 21 as a sign of chronic salpingitis. 22 THE REPORTER: Chronic what? 23 THE WITNESS: Salpingitis, 24 S-A-L-P-I-N-G-I-T-I-S.</p>

<p style="text-align: right;">Page 162</p> <p>1 BY DR. RESTAINO: 2 Q. Okay. When -- when you 3 make -- when you list -- listing here the 4 diagnosis of p53 SIG, did you make that 5 diagnosis or was it made for you already 6 by someone in -- in listing this slide? 7 A. I review the slides and make 8 the diagnosis as listed. 9 Q. You made the diagnosis as 10 it -- or did you confirm the diagnosis 11 that was listed? 12 A. In this study I think I made 13 the final diagnosis. I don't care about 14 what has been written. But I would look 15 at the primary report and they are all 16 consistent. 17 Q. So your diagnosis was 18 consistent with the existing primary 19 diagnoses of these slides? 20 A. I cannot remember I check 21 everyone, okay. But the most important 22 thing is the diagnosis I listed is my 23 final decision. 24 Q. And I'm not trying to</p>	<p style="text-align: right;">Page 164</p> <p>1 lesions in them? 2 A. I just search from the -- 3 from the list we have, contending any 4 tubal lesions or abnormalities like a 5 cancer. 6 As you can see here -- 7 Q. Yes. 8 A. -- it's our brain cancer 9 listed. And that's -- that's what I did. 10 Then I retrieve them, then I review under 11 the microscope, and then I put a 12 diagnosis. 13 Q. And then you were able to 14 confirm the presence of the p53 SIG 15 lesion? 16 MS. MILLER: Objection. 17 THE WITNESS: By myself. 18 BY DR. RESTAINO: 19 Q. And is that the same 20 methodology you did with the STIC 21 lesions, find those slides that had STIC 22 lesions in them, look under the 23 microscope, confirm that there was STIC 24 lesions?</p>
<p style="text-align: right;">Page 163</p> <p>1 confuse you. I'm just trying to be 2 clear. 3 If this is Slide S8001, and 4 you put it under the microscope to look 5 for the p53 signature lesions, is there a 6 report somewhere or a listing somewhere 7 that you say, ah, yes, p53 SIG lesions, 8 and then you look in the microscope and 9 you confirm it? 10 A. Oh, okay. I understand your 11 question. I did not do that. 12 Q. You did not confirm the 13 diagnosis? 14 A. No, I did not see the 15 original diagnosis, but as you know on 16 this page, they must have some diagnosis 17 already. Okay. 18 Q. In other -- 19 A. This says tubal lesions. 20 Q. Okay. 21 A. But I -- I just made the 22 diagnosis by myself. 23 Q. How did you select or know 24 to select the slides that had p53 SIG</p>	<p style="text-align: right;">Page 165</p> <p>1 A. This is not a confirmation 2 study. This is a study to understand 3 chronic inflammation. So I select those 4 abnormal fallopian tube lesions, 5 including cancer or no cancer. Then I 6 make my final diagnosis. 7 Q. How many slides did you have 8 to look at in order to come up with the 9 number of slides that -- in order to come 10 up with the 18 p53 signature lesions, how 11 many slides did you have to go through to 12 find those 18 slides? 13 A. Do you mean from the 14 original or in our list? Because as you 15 need to understand, so this study is all 16 about the tubal lesions. So if there is 17 a normal fallopian tube, usually we did 18 not include in this study, because that's 19 not our purpose. 20 So that means if we include 21 the eligible case or cases in the list, 22 they must have some tubal lesions. 23 Q. Okay. And the -- and the 24 tubal lesions that of interest to you for</p>

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<p style="text-align: right;">Page 166</p> <p>1 your study that you selected were the p53</p> <p>2 SIG lesions, or STIC, correct?</p> <p>3 A. With -- without cancer or</p> <p>4 with cancer.</p> <p>5 Q. Understood. Okay.</p> <p>6 A. I should tell you, the STIC,</p> <p>7 I say here, okay, so without cancer, I</p> <p>8 think the STIC. With cancer, I label</p> <p>9 STIC, but actually it's a STIC-like</p> <p>10 lesion. Because we never know if it's a</p> <p>11 metastases of cancer or it's original</p> <p>12 ones.</p> <p>13 Q. Okay.</p> <p>14 A. So -- so this even for the</p> <p>15 pathologist very confusing, because STIC,</p> <p>16 what do you mean. My definition here is,</p> <p>17 under microscope, if STIC was cancer,</p> <p>18 that is STIC-like lesions. So this apply</p> <p>19 to all the deposition today. It's not</p> <p>20 only STIC, because it's too confusing.</p> <p>21 Q. Do you use the term</p> <p>22 "STIC-like lesions" in your -- in your</p> <p>23 study report?</p> <p>24 A. It depends. I -- I'm sorry,</p>	<p style="text-align: right;">Page 168</p> <p>1 cannot say 40 percent exact.</p> <p>2 Q. If you were to sit for us</p> <p>3 today and estimate for us, what would be</p> <p>4 the estimate of the number of high grade</p> <p>5 serous carcinomas do not have precursor</p> <p>6 cell lesions?</p> <p>7 A. I think this is a question,</p> <p>8 that based on your assumption is a</p> <p>9 precursor. I want to restate your</p> <p>10 question is whether there is a STIC-like</p> <p>11 lesion associated with cancer. Then I</p> <p>12 can answer that question. Because I</p> <p>13 don't know if it is really a precursor or</p> <p>14 not.</p> <p>15 Q. Okay. Now, you state that</p> <p>16 for example, on your Lesion 1, there's no</p> <p>17 inflammation; is that correct?</p> <p>18 A. Correct.</p> <p>19 Q. And the inflammation is</p> <p>20 defined as below, by increased</p> <p>21 lymphocytic infiltrate, correct?</p> <p>22 A. Plus whether there is plicae</p> <p>23 fusion as I mentioned in my methodology</p> <p>24 in my report.</p>
<p style="text-align: right;">Page 167</p> <p>1 say that again.</p> <p>2 Q. Do you use the term</p> <p>3 "STIC-like lesions" in your study report</p> <p>4 that you've performed -- that you have</p> <p>5 produced to us?</p> <p>6 A. I don't think so. I think</p> <p>7 in that way would confuse more people. I</p> <p>8 think it's better for explanation</p> <p>9 colloquially.</p> <p>10 Q. Would you agree that</p> <p>11 approximately 40 percent of high grade</p> <p>12 serous epithelial carcinomas don't have</p> <p>13 precursor cells?</p> <p>14 A. Which type of cancer are you</p> <p>15 talking about?</p> <p>16 Q. HG -- the cancer we are</p> <p>17 talking about, the high grade serous</p> <p>18 epithelial ovarian cancer.</p> <p>19 MS. MILLER: Right there.</p> <p>20 BY DR. RESTAINO:</p> <p>21 Q. Would you agree that</p> <p>22 approximately 40 percent don't have</p> <p>23 precursor cells?</p> <p>24 A. It depends on study, but I</p>	<p style="text-align: right;">Page 169</p> <p>1 Q. Did you observe macrophages</p> <p>2 in that slide?</p> <p>3 MS. MILLER: Objection.</p> <p>4 THE WITNESS: I examine</p> <p>5 inflammatory cells that can</p> <p>6 constitute our pathologic</p> <p>7 diagnosis of chronic inflammation.</p> <p>8 Whatever we are trained, I</p> <p>9 exercise here.</p> <p>10 DR. RESTAINO: Doctor, I'll</p> <p>11 move to strike as unresponsive.</p> <p>12 BY DR. RESTAINO:</p> <p>13 Q. Did you observe macrophages</p> <p>14 in slides with Lesion Number 1?</p> <p>15 A. I examine all the</p> <p>16 inflammatory cells.</p> <p>17 Q. Does that include</p> <p>18 macrophages?</p> <p>19 MS. MILLER: Objection.</p> <p>20 THE WITNESS: If there is</p> <p>21 present. If it is not present, I</p> <p>22 cannot say it.</p> <p>23 BY DR. RESTAINO:</p> <p>24 Q. Did you examine for the</p>

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<p style="text-align: right;">Page 170</p> <p>1 presence of dendritic cells?</p> <p>2 A. Which -- dendritic cells?</p> <p>3 Q. Yes.</p> <p>4 A. This is not in the criteria</p> <p>5 for us to diagnose chronic inflammation.</p> <p>6 Every pathologist who are practicing</p> <p>7 pathology diagnosis, they don't need to</p> <p>8 look at specific cell type to make up the</p> <p>9 inflammation.</p> <p>10 Q. Then why did you look at</p> <p>11 lymphocytes?</p> <p>12 A. Lymphocytes is the most</p> <p>13 important criteria to the pathologists</p> <p>14 who are able to make up, because they are</p> <p>15 most common.</p> <p>16 Q. More common than polynuclear</p> <p>17 cells, polymorphonuclear cells PMNs?</p> <p>18 A. PMN is a component of acute</p> <p>19 inflammation.</p> <p>20 Q. And you observed evidence of</p> <p>21 acute inflammation in your slide</p> <p>22 analysis, didn't you?</p> <p>23 MS. MILLER: Objection.</p> <p>24 THE WITNESS: Yes. And I</p>	<p style="text-align: right;">Page 172</p> <p>1 innate immune system, including</p> <p>2 lymphocytes, B-cells, T-cells, dendritic</p> <p>3 cells, macrophages, PMNs, the sole cell</p> <p>4 type that you decided to look for was</p> <p>5 lymphocytes, correct?</p> <p>6 A. I think --</p> <p>7 MS. MILLER: Objection.</p> <p>8 Please, Dr. Shih.</p> <p>9 THE WITNESS: Can you repeat</p> <p>10 one more time.</p> <p>11 BY DR. RESTAINO:</p> <p>12 Q. So of the components of the</p> <p>13 innate immune system, including</p> <p>14 lymphocytes, beta cells, T-cells,</p> <p>15 dendritic cells, polymorphonucleocytes,</p> <p>16 PMNs, and lymphocytes, the sole type that</p> <p>17 you chose to look for in your -- in this</p> <p>18 study are the lymphocytes, correct?</p> <p>19 A. You said in innate system</p> <p>20 including B -- T-cells. I don't think</p> <p>21 T-cells is part of innate immune system.</p> <p>22 So I don't know what you're</p> <p>23 talking about.</p> <p>24 Q. Okay. Then I'll strike the</p>
<p style="text-align: right;">Page 171</p> <p>1 did not find any acute</p> <p>2 inflammation.</p> <p>3 BY DR. RESTAINO:</p> <p>4 Q. And --</p> <p>5 MS. MILLER: Wait. I think</p> <p>6 you're speaking past each other.</p> <p>7 THE WITNESS: Okay. Can we</p> <p>8 start over again?</p> <p>9 BY DR. RESTAINO:</p> <p>10 Q. Yeah, would you agree that</p> <p>11 chronic inflammation is acute</p> <p>12 inflammation which doesn't go away?</p> <p>13 MS. MILLER: Objection.</p> <p>14 THE WITNESS: Chronic</p> <p>15 inflammation is enriched by</p> <p>16 lymphocytes. They can come in</p> <p>17 from different resources. Like,</p> <p>18 autoimmune disease you don't have</p> <p>19 acute inflammation, but you have</p> <p>20 chronic inflammation. So it</p> <p>21 depends on the context and biology</p> <p>22 and the pathogenesis.</p> <p>23 BY DR. RESTAINO:</p> <p>24 Q. So of the components of the</p>	<p style="text-align: right;">Page 173</p> <p>1 question and I'll ask you this way.</p> <p>2 As part of the immune</p> <p>3 response the cells of the body include</p> <p>4 B-cells, T-cells, PMN, macrophages, and</p> <p>5 lymphocytes, correct?</p> <p>6 A. You can say that.</p> <p>7 Q. Okay. And you chose to look</p> <p>8 for lymphocytes, correct?</p> <p>9 A. No, I said I look for</p> <p>10 inflammatory cells, including</p> <p>11 lymphocytes.</p> <p>12 Q. Okay. Do you list in your</p> <p>13 study anywhere the presence or absence of</p> <p>14 macrophages?</p> <p>15 A. I don't see any prominent</p> <p>16 macrophages at all in those cases.</p> <p>17 Q. And how about PMNs?</p> <p>18 A. I don't see any.</p> <p>19 Q. In any of them, even in --</p> <p>20 if you go down to Lesion Number 14, Slide</p> <p>21 ID 10146, where there's yes under</p> <p>22 inflammation, did you see macrophages?</p> <p>23 A. I think you are talking</p> <p>24 about the STIC or STIC-like lesions. You</p>

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<p style="text-align: right;">Page 174</p> <p>1 are talking about every cases here? I</p> <p>2 just want to make sure that you're</p> <p>3 talking about the whole list.</p> <p>4 Q. In this entire list, do you</p> <p>5 list anywhere -- did you quantitate the</p> <p>6 presence of macrophages?</p> <p>7 A. I cannot recall in ovarian</p> <p>8 cancer I see any macrophages, because</p> <p>9 that -- these cells are not</p> <p>10 characteristics component.</p> <p>11 Q. Of?</p> <p>12 A. Of high grade serous</p> <p>13 carcinoma. Usually they are T-cell,</p> <p>14 B-cell and the plasma cells and these</p> <p>15 other things. So it could be part of it,</p> <p>16 but I did not say it here.</p> <p>17 Q. What about the chronic</p> <p>18 inflammatory process instead of the high</p> <p>19 grade serous carcinoma? Are macrophages</p> <p>20 part of an inflammatory process?</p> <p>21 A. No.</p> <p>22 Q. Are PMNs part of an</p> <p>23 inflammatory process?</p> <p>24 A. In a STIC or STIC-like</p>	<p style="text-align: right;">Page 176</p> <p>1 chronic inflammation.</p> <p>2 A. Okay.</p> <p>3 Q. What are the normal immune</p> <p>4 cells that you as a pathologist would</p> <p>5 look for when making the diagnosis of</p> <p>6 chronic inflammation?</p> <p>7 A. We look at any inflammatory</p> <p>8 cells. Again, okay, so the lymphocyte,</p> <p>9 macrophages and those that we can easily</p> <p>10 identify by H&E slides under microscope,</p> <p>11 we do that. So it's not based on only</p> <p>12 lymphocytes. It's based on macrophages</p> <p>13 and other inflammatory cells taken</p> <p>14 together.</p> <p>15 Q. Okay. Thank you. We'll</p> <p>16 move on.</p> <p>17 Under the case ID column,</p> <p>18 just to clear up some questions, the</p> <p>19 first seven slides are S80001 to S80007.</p> <p>20 Do you see that, sir?</p> <p>21 A. Yes.</p> <p>22 Q. But then the next one is</p> <p>23 10150?</p> <p>24 A. Yeah.</p>
<p style="text-align: right;">Page 175</p> <p>1 lesions?</p> <p>2 Q. In anything?</p> <p>3 A. Well --</p> <p>4 Q. Any inflammation that goes</p> <p>5 on in the body.</p> <p>6 A. Ah, okay.</p> <p>7 Q. Tendinitis from playing too</p> <p>8 much tennis.</p> <p>9 MS. MILLER: Wait a minute.</p> <p>10 Can we have just one question?</p> <p>11 Because now we're having a back</p> <p>12 and forth. I just want to know</p> <p>13 what the question is so I know</p> <p>14 it's objectionable or not, and</p> <p>15 then I want him to answer.</p> <p>16 BY DR. RESTAINO:</p> <p>17 Q. In the body's response to</p> <p>18 inflammation, do the cells include PMN,</p> <p>19 macrophages, lymphocytes, dendritic</p> <p>20 cells? Agreed?</p> <p>21 A. It depends on what type of</p> <p>22 inflammation and the insult and tissue</p> <p>23 type.</p> <p>24 Q. Okay. Let's talk about</p>	<p style="text-align: right;">Page 177</p> <p>1 Q. Why?</p> <p>2 A. Just a different labeling</p> <p>3 system. There's no -- nothing curious.</p> <p>4 Q. Is that your labeling system</p> <p>5 or the way the slides were labeled in the</p> <p>6 tissue -- in the slide bank?</p> <p>7 A. I cannot remember that. My</p> <p>8 job is to pull out the slides and make my</p> <p>9 diagnosis and record my results.</p> <p>10 Q. Couple more down. When I'm</p> <p>11 looking at Lesion 9 and 10, there are two</p> <p>12 slides that have Case ID 10149.</p> <p>13 Do you see that, sir?</p> <p>14 A. 10 --</p> <p>15 Q. 10149. It's Lesion Number</p> <p>16 9, Lesion Number 10?</p> <p>17 A. 9, 10, yes.</p> <p>18 Q. And why are there two IDs --</p> <p>19 same identical IDs assigned to two</p> <p>20 slides?</p> <p>21 A. So I think there's a</p> <p>22 Figure 2, would be important for you.</p> <p>23 You need to understand that ovarian</p> <p>24 cancer lesion here, has multiple lesions</p>

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<p style="text-align: right;">Page 178</p> <p>1 before the cancer develop. That's really</p> <p>2 our really nice study to show to the</p> <p>3 scientists that the fimbriated end of</p> <p>4 fallopian tube contain multiple precursor</p> <p>5 lesions, and our hypothesis is only one,</p> <p>6 or very few, maybe only one, can develop</p> <p>7 into carcinoma.</p> <p>8 So that's why this carcinoma</p> <p>9 can destroy the other -- other tissue in</p> <p>10 the fallopian tube.</p> <p>11 And usually what happens --</p> <p>12 DR. RESTAINO: Sir, I'm</p> <p>13 going to move to strike.</p> <p>14 BY DR. RESTAINO:</p> <p>15 Q. I'm just asking you, why are</p> <p>16 these two slides -- why do they both have</p> <p>17 the same ID number?</p> <p>18 A. They have Signature 1 and</p> <p>19 Signature 2. Can you see that?</p> <p>20 Q. I see that.</p> <p>21 A. Yeah. So there's one here,</p> <p>22 two here. These are discrete lesions for</p> <p>23 the same patient. Is that clear?</p> <p>24 Q. Okay, sir.</p>	<p style="text-align: right;">Page 180</p> <p>1 already.</p> <p>2 MS. MILLER: Objection.</p> <p>3 Asked and answered.</p> <p>4 Please, Dr. Shih, give me</p> <p>5 five seconds. I'll give up on ten</p> <p>6 seconds. I'm asking now for five.</p> <p>7 THE WITNESS: Okay.</p> <p>8 BY DR. RESTAINO:</p> <p>9 Q. I'm sorry, I keep asking the</p> <p>10 question. I still don't understand who</p> <p>11 came up with that case ID number, you or</p> <p>12 was it an existing ID number?</p> <p>13 A. I cannot recall.</p> <p>14 Q. Okay. And would it be the</p> <p>15 same thing, like for example, if you go</p> <p>16 down to the last four instead of the</p> <p>17 numbers that we've been seeing above, now</p> <p>18 all of the sudden we have 20001 NFT.</p> <p>19 Do you see that, sir?</p> <p>20 A. Yes.</p> <p>21 Q. Who came up with that</p> <p>22 number, you or somebody else?</p> <p>23 A. These four cases, NFT, do</p> <p>24 you know what is NFT? Normal fallopian</p>
<p style="text-align: right;">Page 179</p> <p>1 A. Okay.</p> <p>2 Q. So 10149, that would refer</p> <p>3 to the same patient?</p> <p>4 A. Correct.</p> <p>5 Q. Okay. Thank you.</p> <p>6 And then going down -- and</p> <p>7 I'm not going to go through all these</p> <p>8 different questions because I think I</p> <p>9 understand now.</p> <p>10 These numbers, the case ID</p> <p>11 number, you didn't assign that case</p> <p>12 number to a particular slide. That was</p> <p>13 the existing case number for that slide;</p> <p>14 is that correct?</p> <p>15 MS. MILLER: Objection. I</p> <p>16 thought he said he didn't know.</p> <p>17 THE WITNESS: I think I</p> <p>18 answered your question.</p> <p>19 BY DR. RESTAINO:</p> <p>20 Q. For the very first slide,</p> <p>21 Lesion 1, S8001, did you make up that</p> <p>22 case ID number?</p> <p>23 MS. MILLER: Objection.</p> <p>24 THE WITNESS: I told you</p>	<p style="text-align: right;">Page 181</p> <p>1 tube.</p> <p>2 Q. Okay.</p> <p>3 A. So, as in my report, if you</p> <p>4 read it, it says that in order to come</p> <p>5 out with control and we combine the</p> <p>6 previous study in Ardighieri study and</p> <p>7 the new cases of fallopian tube, so</p> <p>8 that's -- we randomly select from our</p> <p>9 file of the normal fallopian tube to be</p> <p>10 included.</p> <p>11 Q. Okay. So therefore, with</p> <p>12 those four, when you sat down at the</p> <p>13 microscope and you took the histology</p> <p>14 slide 2001 NFT, you knew that the</p> <p>15 previous -- or the preexisting diagnosis</p> <p>16 was normal fallopian tube, correct?</p> <p>17 A. In our diagnosis, we say</p> <p>18 histologically unremarkable.</p> <p>19 Q. Yes, but who made the</p> <p>20 initial diagnosis of normal fallopian</p> <p>21 tube leading to the case ID 20001 NFT?</p> <p>22 A. I don't know. It's for our</p> <p>23 files.</p> <p>24 Q. Okay. In conducting a</p>

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<p style="text-align: right;">Page 182</p> <p>1 research study such as this one or any</p> <p>2 other that you have done in the past and</p> <p>3 published, there are studies where you</p> <p>4 describe yourself as being blinded to</p> <p>5 preexisting information and looking at a</p> <p>6 slide for the first time, correct? Do</p> <p>7 you understand what I mean by blinded?</p> <p>8 A. In some studies.</p> <p>9 Q. Yes. And what's the reason</p> <p>10 for blinding in some studies?</p> <p>11 A. The blinded study are</p> <p>12 important for the correlation with</p> <p>13 clinical outcome. Like survival,</p> <p>14 resistant to chemotherapy, et cetera.</p> <p>15 And we usually, what happens is for this</p> <p>16 blinded, so we have clinical data about</p> <p>17 clinical outcome, and a pathology review</p> <p>18 the slides without knowing the clinical</p> <p>19 outcome. So I think these are blinded</p> <p>20 studies.</p> <p>21 Q. Okay.</p> <p>22 A. Because when you look at</p> <p>23 pathology slides, you are not a</p> <p>24 diagnosis, it cannot be blinded. So it</p>	<p style="text-align: right;">Page 184</p> <p>1 definition.</p> <p>2 Q. What is your definition,</p> <p>3 sir?</p> <p>4 A. Meaning if you know</p> <p>5 something like a clinical outcome that</p> <p>6 will affect your interpretation of the</p> <p>7 result. But for the pathology diagnosis</p> <p>8 it's black and white. You cannot -- you</p> <p>9 don't have discount bias.</p> <p>10 Because if we have a bias in</p> <p>11 pathology practice, then what happened to</p> <p>12 the patient's diagnosis, right?</p> <p>13 Okay. So for example, we</p> <p>14 have a tissue, perform a biopsy on a</p> <p>15 woman with a lump in the breast. We want</p> <p>16 to know, woman here want to know if this</p> <p>17 is benign or malignant. We can answer,</p> <p>18 oh, this is malignant. So we -- we</p> <p>19 change our diagnosis or set our mind to</p> <p>20 this opinion. No.</p> <p>21 This is really breach the --</p> <p>22 the pathology practice. So a pathologist</p> <p>23 is evidence based. It's different</p> <p>24 information like data and -- and risk</p>
<p style="text-align: right;">Page 183</p> <p>1 is different form of research designs.</p> <p>2 Q. When a -- when a pathologist</p> <p>3 is blinded for specific studies, that's</p> <p>4 to reduce bias, correct?</p> <p>5 MS. MILLER: Objection.</p> <p>6 THE WITNESS: Can you say</p> <p>7 that again?</p> <p>8 BY DR. RESTAINO:</p> <p>9 Q. The use of blinding is to</p> <p>10 reduce the potential for bias --</p> <p>11 MS. MILLER: Object again --</p> <p>12 BY DR. RESTAINO:</p> <p>13 Q. -- agreed?</p> <p>14 MS. MILLER: I'm sorry.</p> <p>15 Objection.</p> <p>16 THE WITNESS: What kind of</p> <p>17 bias you -- you are talking about?</p> <p>18 BY DR. RESTAINO:</p> <p>19 Q. How about, are you familiar</p> <p>20 with the term "confirmation bias"?</p> <p>21 A. Maybe.</p> <p>22 Q. You don't know?</p> <p>23 A. I know. But I don't know</p> <p>24 what that mean to you, but I have my own</p>	<p style="text-align: right;">Page 185</p> <p>1 factors and this and that because they</p> <p>2 can really bias.</p> <p>3 Pathology, it's really black</p> <p>4 and white. Otherwise what pathology</p> <p>5 diagnosis need to exist in medical</p> <p>6 system? So pathology is a finite</p> <p>7 diagnosis. You cannot change -- you</p> <p>8 cannot challenge that.</p> <p>9 Q. And bias is a form of</p> <p>10 confounding, correct?</p> <p>11 A. It depends what you mean.</p> <p>12 Could you be more specific for that?</p> <p>13 Q. Do you understand --</p> <p>14 understand the word confounding as it's</p> <p>15 used in science?</p> <p>16 A. So my confounding definition</p> <p>17 is some factors, they are not driving,</p> <p>18 but they are associated with the outcome.</p> <p>19 For example, in many epidemiology</p> <p>20 studies, especially those with very low</p> <p>21 risk, 1.3, they are full of confounding</p> <p>22 factors.</p> <p>23 Q. Right. Would that hold true</p> <p>24 for passive smoking and lung cancer,</p>

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<p style="text-align: right;">Page 186</p> <p>1 which has an odds ratio of 1.3?</p> <p>2 A. Can you say that one more</p> <p>3 time?</p> <p>4 Q. Would that hold true also</p> <p>5 for passive smoking and lung cancer which</p> <p>6 has an odds ratio of 1.3?</p> <p>7 A. I am not the expert in that</p> <p>8 field. So I cannot answer your question.</p> <p>9 I am here to answer the</p> <p>10 causal relationship of talc, including</p> <p>11 Johnson & Johnson powder, whether it</p> <p>12 cause ovarian cancer, any biological</p> <p>13 plausibility.</p> <p>14 Q. What steps did you take in</p> <p>15 conducting your study to rule out</p> <p>16 confounders?</p> <p>17 A. Which -- which study?</p> <p>18 Q. The study we are talking</p> <p>19 about, the study that you have produced</p> <p>20 to us, what steps have you taken to rule</p> <p>21 out confounding elements?</p> <p>22 MS. MILLER: Objection.</p> <p>23 THE WITNESS: So your</p> <p>24 question is, what are the</p>	<p style="text-align: right;">Page 188</p> <p>1 us what -- what the word lymphocytopenia</p> <p>2 means?</p> <p>3 A. Could you spell it for me?</p> <p>4 Q. As a physician and</p> <p>5 pathologist, you don't recognize the word</p> <p>6 lymphocytopenia?</p> <p>7 A. Lymphocytopenia.</p> <p>8 Q. Lymphocytopenia.</p> <p>9 A. That means -- okay. If I</p> <p>10 understand your pronunciation correctly.</p> <p>11 Means -- penia means deficient or lower.</p> <p>12 The less means. Lymphocyte has reduced</p> <p>13 their number in circulation.</p> <p>14 Q. Only in circulation?</p> <p>15 A. That's what I understand.</p> <p>16 Usually people use that term in cancer</p> <p>17 patient after chemotherapy.</p> <p>18 Q. If a patient has documented</p> <p>19 lymphocytopenia as determined from a --</p> <p>20 from blood test, and decreased</p> <p>21 lymphocytes circulating in the blood and</p> <p>22 serum, would you also expect to see less</p> <p>23 lymphocytes at sites of inflammation?</p> <p>24 A. So again, I tell you</p>
<p style="text-align: right;">Page 187</p> <p>1 confounding factors in this study?</p> <p>2 BY DR. RESTAINO:</p> <p>3 Q. No, sir. What steps did you</p> <p>4 take to rule out confounding factors?</p> <p>5 A. Okay. I don't have any</p> <p>6 pre-set mind whether ovarian cancer</p> <p>7 precursors, including p53 signature and</p> <p>8 STIC without cancer is inflammatory or</p> <p>9 not, because if yes or no, they are big</p> <p>10 deal in this field. They are equally</p> <p>11 exciting in the biological studies. So I</p> <p>12 welcome any good results that can show</p> <p>13 convincingly yes or no.</p> <p>14 If yes, we can do a whole</p> <p>15 set of new studies, quite exciting. And</p> <p>16 the -- the opposite is true, if there is</p> <p>17 no inflammation, we just direct to the</p> <p>18 other research field to answer what is</p> <p>19 the course, the biological basis of</p> <p>20 ovarian high grade serous carcinoma.</p> <p>21 DR. RESTAINO: I'll move to</p> <p>22 strike as nonresponsive.</p> <p>23 BY DR. RESTAINO:</p> <p>24 Q. Doctor, can you define for</p>	<p style="text-align: right;">Page 189</p> <p>1 already -- I have told you already, that</p> <p>2 two claims whether there is chronic</p> <p>3 inflammation as shown in this Table 2,</p> <p>4 it's based on not on the absolute number</p> <p>5 of lymphocytes I see as compared to the</p> <p>6 adjacent normal or histologically</p> <p>7 unremarkable mucosa as compared.</p> <p>8 If there is a cyto --</p> <p>9 lymphocytopenia, okay, so you should be</p> <p>10 able to see increased number as compared</p> <p>11 to the normal mucosa for the same</p> <p>12 leukopenia patient.</p> <p>13 Q. Unless there were</p> <p>14 confounding factors present, correct?</p> <p>15 A. Say that again.</p> <p>16 Q. Unless there were</p> <p>17 confounding factors present, like, for</p> <p>18 example lymphocytopenia. And if one had</p> <p>19 lymphocytopenia that was drug-induced</p> <p>20 from example for the anti --</p> <p>21 chemotherapeutic Imuran, I-M-U-R-A-N,</p> <p>22 azathioprine, then if that patient has</p> <p>23 drug-induced lymphocytopenia, regardless</p> <p>24 of what tissue you look at, there's going</p>

<p style="text-align: right;">Page 190</p> <p>1 to be a decreased number of lymphocytes 2 present, isn't there? 3 A. Yeah, but that will not 4 affect my chronic inflammation diagnosis. 5 I use the comparison to the same area. 6 Okay. So if in the normal, 7 it's 100, and we have 300 in the STIC, 8 that's chronic inflammation. In the 9 leukocytopenia, if you only can count 50, 10 okay. It's lower, right? 11 Leukocytopenia, right, 50. Now if you 12 count 100, now you still call it chronic 13 inflammation. 14 So it's relative, rather 15 than -- so I don't think this is a 16 confounding factor at all. 17 Q. How many of the women from 18 whom these slides were obtained were on 19 azathioprine? 20 A. What is that? Can you spell 21 it for me. 22 Q. A-Z-A-T-H-I-O-P-R-I-N-E. 23 The generic name that -- the brand name 24 is Imuran, I-M-U-R-A-N, or Azasan</p>	<p style="text-align: right;">Page 192</p> <p>1 review the -- under the microscope to see 2 whether there is increased inflammation 3 as compared to the adjacent normal tissue 4 from the same patient, no matter what he 5 actually take. 6 Q. How many patients took 7 cimetidine over-the-counter, also known 8 as Tagamet? 9 A. Could you spell the. 10 Q. Cimetidine is 11 C-I-M-E-T-I-D-I-N-E. Tagamet. Do you 12 know how many of them took Tagamet 13 over-the-counter? 14 A. This is not relevant to our 15 discussion. 16 Q. Do you know if Tagamet is 17 associated with lymphocytopenia? 18 A. As we discussed, cytopenia 19 is not a confounding factor in my study. 20 Q. Are you familiar with the 21 class of drugs known as the 22 corticosteroids? 23 A. I know the name, but could 24 you specify which corticosteroids we're</p>
<p style="text-align: right;">Page 191</p> <p>1 A-Z-A-S-A-N. They are cancer therapeutic 2 agents. 3 A. I'm a pathologist. I am not 4 a medical oncologist. 5 Q. Do you know if those drugs 6 can cause lymphocytopenia? 7 A. I am a pathologist. I am 8 not a medical oncologist to have this 9 knowledge. 10 Q. How many of the women from 11 whom these slides were obtained were on 12 carbamazepine, also known as Tegretol, 13 used to treat seizures, nerve pain, 14 bipolar disorders. How many patients 15 suffered from those conditions and was on 16 carbamazepine, also known as Tegretol? 17 A. I don't think this 18 information is relevant to my study and 19 my conclusion at this moment. 20 Q. Is -- do you know if 21 carbamazepine causes lymphocytopenia? 22 A. Again, I'm not medical 23 oncologist. I did not directly take care 24 of the patients. I -- my job is to</p>	<p style="text-align: right;">Page 193</p> <p>1 talking about. There are so many 2 different kinds for different -- 3 Q. The class itself is known as 4 anti -- or is known as antiinflammatory 5 drugs, correct? 6 A. Again, I'm not the 7 first-line medical doctor. I'm a 8 pathologist. So -- and most importantly, 9 I think your questions are not relevant 10 to my study. 11 Q. If a patient had rheumatic 12 fever -- excuse me -- has rheumatoid 13 arthritis and was taking prednisone for 14 that condition, prednisone, a 15 corticosteroid, is an antiinflammatory 16 agent, correct? 17 A. Again, this is also not in 18 my opinion and my expertise. 19 Q. Okay. Are you familiar with 20 methotrexate? 21 A. I think my answer is the 22 same. This is not relevant. It's not 23 confounding factors, because I diagnose 24 chronic inflammation in my -- in my</p>

<p style="text-align: right;">Page 194</p> <p>1 specimens based on comparison, based on 2 comparison of the -- whether there is 3 chronic inflammation associated with p53 4 signature, STIC, and the adjacent normal 5 tissue at the same time, as I give you 6 the example. Normal patient is 100 -- so 7 100, you get 300, then you have chronic 8 inflammation. 9 Now if the patient take 10 methotrexate, steroid, whatever that 11 cause leukopenia, it will reduced from 12 100 to 60. Okay. Then if I see is 80 or 13 100 in the STIC, and then I will call it 14 chronic inflammation. 15 So this is definitely not 16 confounding factors because of my study 17 design. 18 Q. Sir, if you look at your 19 Table 2, and we'll just look at Lesion 20 Number 7. 21 DR. RESTAINO: I'm going to 22 move to strike your previous 23 answer as unresponsive. 24 BY DR. RESTAINO:</p>	<p style="text-align: right;">Page 196</p> <p>1 Q. Is that the way you did it? 2 A. That's only one way. 3 Q. What else did you do? 4 A. The other way is to compare 5 to the NFT, as you just mentioned in the 6 inquiry. And so we have two references. 7 Q. For the same patient? 8 A. Different patients. 9 Q. So -- 10 A. We compare same patients and 11 also compare two different patients. 12 Q. So you're comparing the 13 presence and quantifying the inflammatory 14 process in Patient A to Patient B who has 15 normal fallopian tube, and making a 16 comparison; is that true? 17 A. I think you have a wrong 18 statement. I did not quantify. Again, I 19 used the pathology knowledge and 20 background and training, experience, to 21 make the chronic inflammation. 22 We did not really count one 23 by one; otherwise, the pathology practice 24 in every hospital will come to a halt.</p>
<p style="text-align: right;">Page 195</p> <p>1 Q. Let's look at Lesion Number 2 7. It's a STIC lesion, no concurrent 3 cancer, no inflammation, correct? 4 A. Number 7 you mean? The 5 number is S -- 6 Q. Yes, it's S80007. Okay. 7 That was a histology slide that had 8 evidence of a STIC lesion in it, correct? 9 A. I saw it. 10 Q. Okay. What slide did you 11 compare that against? 12 A. The same slide, because 13 remember, this is a Figure 2. The STIC 14 is only a microscopic focus. It is very 15 small. You cannot see it in the gross. 16 So it only occupies less than one percent 17 of the tissue I examined. So there's a 18 99 percent -- at least 99 percent more 19 histologically unremarkable. 20 Q. Okay. So you're comparing 21 the STIC lesion in that slide compared to 22 the normal tissue in that same slide? Is 23 that my understanding? 24 A. That is one way.</p>	<p style="text-align: right;">Page 197</p> <p>1 Q. Sir, would you expect to see 2 increased lymphocytes, PMNs, macrophages, 3 any of the inflammatory cells with the 4 normal fallopian tubal tissue? 5 MS. MILLER: Objection. 6 THE WITNESS: It depends. 7 BY DR. RESTAINO: 8 Q. What does it depend upon? 9 A. If there is ectopic 10 pregnancy, okay, you know, ectopic 11 pregnancy in the fallopian tube, it is 12 ruptured, and it will cause inflammation. 13 Q. Okay. That wouldn't be a 14 normal fallopian slide, though, would it? 15 A. No, no, I would not review 16 that. 17 Q. Okay. So I'll ask the 18 question again. In comparing the 19 inflammatory infiltrate that you define 20 as lymphocytic, increased lymphocytic 21 infiltrate, in comparing that with normal 22 tissue -- 23 A. What do you mean "normal 24 tissue"?</p>

<p style="text-align: right;">Page 198</p> <p>1 Q. The normal fallopian tissue.</p> <p>2 A. Okay.</p> <p>3 Q. NFT. Okay. So I believe I</p> <p>4 understood you that you said in one slide</p> <p>5 you look at the STIC lesion and you</p> <p>6 looked at the normal tissue; is that</p> <p>7 correct?</p> <p>8 A. From the same specimen.</p> <p>9 Q. Okay. And you compare the</p> <p>10 presence of the inflammatory lymphocytes</p> <p>11 around the STIC lesion, if there was any,</p> <p>12 with the normal tissue, correct?</p> <p>13 A. For the same patients?</p> <p>14 Q. Yes?</p> <p>15 A. I did that way, yes.</p> <p>16 Q. Now, why would you expect to</p> <p>17 see inflammatory cells around normal</p> <p>18 fallopian tissue if there is no disease</p> <p>19 process going on?</p> <p>20 MS. MILLER: Objection.</p> <p>21 THE WITNESS: I cannot</p> <p>22 understand your question. One</p> <p>23 more time.</p> <p>24 BY DR. RESTAINO:</p>	<p style="text-align: right;">Page 200</p> <p>1 MS. MILLER: Objection.</p> <p>2 BY DR. RESTAINO:</p> <p>3 Q. Now, if that lady was on</p> <p>4 Tagamet, you wouldn't expect to see a</p> <p>5 decrease in the normal fallopian tissue</p> <p>6 because they are not there. But you</p> <p>7 would expect to see decreased lymphocytes</p> <p>8 around the STIC lesion because that's</p> <p>9 what lymphopenia leads to, or</p> <p>10 corticosteroids lead to, are decreased</p> <p>11 inflammatory cells, correct?</p> <p>12 MS. MILLER: Objection.</p> <p>13 THE WITNESS: I think</p> <p>14 there's many typo errors. I</p> <p>15 cannot read this.</p> <p>16 Could you repeat your</p> <p>17 question?</p> <p>18 BY DR. RESTAINO:</p> <p>19 Q. There are typo errors where?</p> <p>20 MS. MILLER: He was trying</p> <p>21 to read the realtime and the</p> <p>22 realtime is -- because there are</p> <p>23 so many complicated words --</p> <p>24 THE WITNESS: I think you</p>
<p style="text-align: right;">Page 199</p> <p>1 Q. If you looked at the</p> <p>2 normal -- if you looked at the bottom</p> <p>3 slide, Number 59, 2004 NFT, with no</p> <p>4 concurrent cancer, no inflammation, you</p> <p>5 looked at the fallopian tube tissue and</p> <p>6 it's normal, you wouldn't expect to see</p> <p>7 increased lymphocytic cells, correct?</p> <p>8 A. I did not see increased</p> <p>9 inflammation as compared to control.</p> <p>10 Q. Which control?</p> <p>11 A. Ovarian cancer.</p> <p>12 Q. Okay. So now if you don't</p> <p>13 see increased inflammation around the</p> <p>14 normal fallopian tube, now you look at</p> <p>15 the STIC lesion to see if there's</p> <p>16 increased lymphocyte infiltrate, correct?</p> <p>17 A. Yes.</p> <p>18 Q. And you compare the two.</p> <p>19 How many lymphocytes are around the</p> <p>20 normal tissue, how many lymphocytes are</p> <p>21 around from the STIC lesion?</p> <p>22 A. From the same specimen.</p> <p>23 Q. Yes. Okay? Agreed? And</p> <p>24 that's what you did.</p>	<p style="text-align: right;">Page 201</p> <p>1 speak too fast. I'm sorry. I --</p> <p>2 even the specialist cannot</p> <p>3 understand what you are talking</p> <p>4 about. I'm sorry.</p> <p>5 BY DR. RESTAINO:</p> <p>6 Q. What I believe you did in</p> <p>7 this study, sir, was look at slides that</p> <p>8 were designated as having p53 signature</p> <p>9 lesions in them, or STIC, or cancer, and</p> <p>10 you compared the inflammation, if it was</p> <p>11 there, around those lesions, with normal</p> <p>12 tissue, correct?</p> <p>13 MR. LOCKE: Objection.</p> <p>14 BY DR. RESTAINO:</p> <p>15 Q. Correct?</p> <p>16 A. From the same patient?</p> <p>17 Q. Whatever you did in this</p> <p>18 study. Whether it was in the same slide,</p> <p>19 or -- let me ask you this.</p> <p>20 Why would you compare the</p> <p>21 number of lymphocytes around a STIC</p> <p>22 lesion in Patient A and compare her with</p> <p>23 the number of lymphocytes in Patient B?</p> <p>24 A. Ah, okay. I think you are</p>

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<p>1 more clear now.</p> <p>2 So this normal fallopian</p> <p>3 tubes without STICs, without cancer, it's</p> <p>4 just a control. It's not the point we</p> <p>5 want to study, okay. So I want to make</p> <p>6 sure that our -- my reference in</p> <p>7 pathology interpretation is correct. I</p> <p>8 use a normal fallopian tube that has been</p> <p>9 shown in the patient's medical record</p> <p>10 showing there's no evidence of</p> <p>11 morphologically remarkable lesions.</p> <p>12 So if I see -- okay, just in</p> <p>13 case. If I see chronic inflammation in</p> <p>14 NFT by which in the medical record did</p> <p>15 not -- did show -- did not show that,</p> <p>16 then I need to have this serve as a</p> <p>17 calibration of my methodology and my</p> <p>18 methods. So it's as a control. Yeah.</p> <p>19 It's not the studies --</p> <p>20 Q. I'm sorry.</p> <p>21 So when you're comparing the</p> <p>22 noncontrol slide with the control, what</p> <p>23 do you know about that control -- the</p> <p>24 noncontrol slide's patient's medical</p>	<p>1 MS. MILLER: I was going to</p> <p>2 try to push through till one, but</p> <p>3 we can quit now.</p> <p>4 DR. RESTAINO: I can go --</p> <p>5 ask a few more questions.</p> <p>6 BY DR. RESTAINO:</p> <p>7 Q. Now, sir, when did you start</p> <p>8 doing your study?</p> <p>9 A. Which study?</p> <p>10 Q. The study that we've been</p> <p>11 discussing all morning?</p> <p>12 A. Again, this study, I would</p> <p>13 say this research project. Okay. So</p> <p>14 it's different. It's like STIC-like</p> <p>15 lesion and STIC, we have a different</p> <p>16 opinion, so that causes confusion in the</p> <p>17 previous transcript that come to my</p> <p>18 notice.</p> <p>19 Q. Okay. If you pick up</p> <p>20 Exhibit Number 4.</p> <p>21 A. Number 4.</p> <p>22 Q. Which is your study report.</p> <p>23 A. Yes.</p> <p>24 Q. Okay. Look at the first</p>
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<p>1 history?</p> <p>2 Did this patient have</p> <p>3 medical disorders leading to</p> <p>4 lymphocytopenia? Did this patient take</p> <p>5 medications that led to lymphocytopenia?</p> <p>6 You don't know that, do you, sir?</p> <p>7 MS. MILLER: Objection.</p> <p>8 Asked and answered multiple times.</p> <p>9 THE WITNESS: I already</p> <p>10 ask -- I already answered this</p> <p>11 question many, many times. Do you</p> <p>12 want me to repeat? I'm happy to.</p> <p>13 BY DR. RESTAINO:</p> <p>14 Q. I don't believe you've</p> <p>15 answered it. The record --</p> <p>16 A. I do, I do. I do. Look at</p> <p>17 the transcript.</p> <p>18 Q. The record will speak for</p> <p>19 itself.</p> <p>20 A. Look at the transcript.</p> <p>21 Please look at the transcript.</p> <p>22 DR. RESTAINO: Okay. Is</p> <p>23 lunch here? Shall we break for</p> <p>24 lunch at this point?</p>	<p>1 page.</p> <p>2 A. Yes.</p> <p>3 Q. Time frame January 1st,</p> <p>4 2019. On January 1st, New Year's Day, is</p> <p>5 that when you started some part of this</p> <p>6 study? What did you do, January 1st,</p> <p>7 19 -- sorry. January 1st, 1953, is my</p> <p>8 birthday.</p> <p>9 January 1st, 2019. What did</p> <p>10 you do on New Year's Day?</p> <p>11 MS. MILLER: Objection.</p> <p>12 THE WITNESS: I celebrate</p> <p>13 the new year.</p> <p>14 BY DR. RESTAINO:</p> <p>15 Q. Okay. What part -- what did</p> <p>16 you do for the study here on January 1st</p> <p>17 of 2019?</p> <p>18 A. I start searching the</p> <p>19 eligible work cases.</p> <p>20 Q. Okay. And at that point you</p> <p>21 were a retained expert for Johnson &</p> <p>22 Johnson?</p> <p>23 A. Correct.</p> <p>24 Q. Where in your study report</p>

<p style="text-align: right;">Page 206</p> <p>1 do -- do you disclose that you're a paid 2 litigation expert for Johnson & Johnson? 3 A. In this Exhibit 4? 4 Q. Yes. 5 A. This was not paid by J&J at 6 all. I think this is our continuation of 7 our research discovery, and we want to 8 understand pathogenesis of ovarian cancer 9 to help women. 10 Q. Okay. When you submit this 11 paper for publication, do you not believe 12 it's going to be required of you to 13 disclose that you were an expert for 14 Johnson & Johnson? 15 MS. MILLER: Objection. He 16 never said that. 17 THE WITNESS: I'm 18 distracted. 19 BY DR. RESTAINO: 20 Q. I'll ask it -- 21 MS. MILLER: Sorry. I 22 didn't mean to distract you. 23 BY DR. RESTAINO: 24 Q. I'll ask the question again,</p>	<p style="text-align: right;">Page 208</p> <p>1 THE WITNESS: So if in my 2 future manuscript submitted to the 3 journal for the consideration of 4 publication, if I talk about 5 talcum powder, including Johnson & 6 Johnson products, and I cite any 7 reference -- references related to 8 talcum powder, I will disclose it 9 and I will say this study was not 10 sponsored by J&J. 11 This is very, very 12 important. This -- this is 13 so-called ethics in publication. 14 And like some study like Saed he 15 did not disclose during the 16 submission, which is totally 17 trigger the suspicion of 18 misconduct. 19 BY DR. RESTAINO: 20 Q. Did you -- did you review 21 for your opinion that you just testified, 22 his draft report or the final published 23 article? 24 A. Both.</p>
<p style="text-align: right;">Page 207</p> <p>1 differently. 2 In the study report that 3 you've attached to your expert report 4 that you describe in your expert report 5 as the full report, where is the 6 disclosure? 7 A. I'm sorry -- 8 MS. MILLER: Objection. 9 THE WITNESS: -- you say 10 full report? This is not a full 11 study yet. 12 BY DR. RESTAINO: 13 Q. Okay. Sir, we went through 14 that before. And it's listed in your 15 expert report wherein you state, "The 16 full report is attached to the back of my 17 expert report." 18 A. At that time, yes. 19 Q. Okay. So where in this 20 report is your disclosure, your conflict 21 of interest disclosure, that at the time 22 you've been conducting this study you are 23 a paid expert for Johnson & Johnson? 24 MS. MILLER: Objection.</p>	<p style="text-align: right;">Page 209</p> <p>1 Q. And in his final published 2 article, does he state that he's a paid 3 expert? 4 A. Can I have the reference to 5 further discuss? Because I need to read 6 whether he -- how he disclose it. 7 Q. It's listed in your expert 8 report. As you sit here today, do you 9 not recall how he -- how he lists -- 10 A. I would like to see the 11 documents. Do you have that? Dr. Saed? 12 Dr. Saed's 2019? It is a really 13 important point. I will show you the 14 contrast, how I did it right. 15 Q. How you did it right? Where 16 did you do it at all? 17 A. I'm sorry, sir? 18 Q. Where did you do it at all? 19 Where in this full report did you 20 disclose that you are an expert for 21 Johnson & Johnson? 22 A. I was saying -- 23 MS. MILLER: Objection. 24 I've got to object to this. This</p>

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<p>1 report was attached to an expert 2 report which has only been 3 submitted to plaintiffs, who 4 obviously know he is an expert. 5 This is just an incredibly 6 unfair line of questioning. 7 THE WITNESS: I said I will 8 disclose it when I submit to the 9 journal editor for publication. 10 Okay. So this -- 11 BY DR. RESTAINO: 12 Q. But your criticism of 13 Dr. Saed was on his nonpublished draft. 14 Did you -- did you look at his final 15 published article with his declaration? 16 A. So the point is, as I serve 17 in editorial boards to review many, many 18 papers, and I also serve as 19 editor-in-chief in a medical magazine, so 20 whoever submitted for review, okay, it 21 should be disclosed. 22 Do you know why? It's so 23 important for the reviewers to judge 24 whether there is any conflict of interest</p>	<p>1 MS. MILLER: Great. 2 THE WITNESS: Okay. Good. 3 THE VIDEOGRAPHER: The time 4 is 1:01 p.m. we're going off the 5 record. 6 - - - 7 (Lunch break.) 8 - - - 9 AFTERNOON SESSION 10 - - - 11 THE VIDEOGRAPHER: The time 12 is 1:35 p.m. And we're back on 13 the record. 14 - - - 15 EXAMINATION (Cont'd.) 16 - - - 17 BY DR. RESTAINO: 18 Q. Welcome back, Dr. Shih. 19 A. Thank you. 20 Q. When we broke, we were 21 finishing up our discussion with the 22 Dr. Saed, et al., study, correct? 23 A. Correct. 24 Q. And you asked to see the</p>
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<p>1 during the review process. 2 Q. Okay. Did Dr. Saed on his 3 final published article declare the 4 following potential conflicts of interest 5 with respect to research, authorship, 6 and/or publication to this article: 7 "Dr. Saed has served as a paid consultant 8 and expert witness in the talcum powder 9 litigation"? 10 MS. MILLER: Objection. 11 BY DR. RESTAINO: 12 Q. Did he disclose that? 13 MS. MILLER: Objection. 14 Dr. Shih has asked multiple times 15 could he see the study so he can 16 answer the question accurately. 17 And you're refusing to show it to 18 him. If we go off the record, I 19 can get a copy of it if you don't 20 have it. 21 DR. RESTAINO: Why don't we 22 just break for lunch, and we'll 23 come back and he can take a look 24 at it. Want to do that?</p>	<p>1 study. We were able to get a copy of it, 2 which I'll now mark as exhibit next. 3 (Document marked for 4 identification as Exhibit 5 Shih-39.) 6 (Whereupon, a discussion was 7 held off the record.) 8 BY DR. RESTAINO: 9 Q. Doctor, have you seen that 10 publication before? 11 A. This publication? 12 Q. Yes, sir. 13 A. Yes, I did. 14 Q. And now if you would look at 15 the Page 9 where the authors have their 16 declaration of conflicting interests. 17 Do you see that, sir? 18 A. Yes. 19 Q. "The authors declared the 20 following potential conflicts of interest 21 with respect to research, authorship, 22 and/or publication of this article." 23 And, "Dr. Saed has served as a paid 24 consultant and expert witness in the</p>

<p style="text-align: right;">Page 214</p> <p>1 talcum powder litigation." 2 Did I read that correctly, 3 sir? 4 A. Yes, they are showing in the 5 paper. 6 Q. Sir, is it -- as you sit 7 here today, having read that, is it still 8 your opinion that Dr. Saed's disclosure 9 is inadequate? 10 A. I believe this is inadequate 11 because this disclosure need to be 12 submitted in the time during the peer 13 review process, because that's most 14 important factor affecting the reviewers' 15 opinion, whether -- how this study is 16 supported and what other biased can be 17 generated in this report. 18 I think it's really 19 important. And as I reviewed his 20 deposition I was provided by J&J law 21 firm, and at that time, I don't see this 22 statement. And also I learn from other 23 expert reports, and I know that there is 24 a serious problem because Dr. Saed</p>	<p style="text-align: right;">Page 216</p> <p>1 that disclosure, correct? 2 MS. MILLER: Objection. 3 THE WITNESS: Can you say 4 that one more time, slowly? 5 BY DR. RESTAINO: 6 Q. So any -- any investigator, 7 any researcher, any physician, who pulls 8 the article to review the article will 9 see the disclosure that you're looking 10 at, correct? 11 A. Correct. 12 Q. And the purpose of such a 13 disclosure, is to allow then that reader 14 to make up his or her own mind as for the 15 potential of bias, correct? 16 A. I cannot agree, because the 17 purpose of peer review system, as you 18 know, is the theater that the publisher 19 can select the good articles, no biased, 20 no -- without any conflict of interest to 21 present to the audience who did not know 22 what happens before. 23 But this clearly is not the 24 case, because there's two parts. One is</p>
<p style="text-align: right;">Page 215</p> <p>1 testified that he was paid for writing 2 this articles. 3 And as you know, this is a 4 job for any academic professor or staff, 5 that's their job, to write articles, 6 because for their scientific discovery 7 and exposure, rather than is supported by 8 any parties outside of academic. 9 So I think clearly, as a 10 editor-in-chief, I served that before, I 11 will be really shocked about this late 12 disclosure. 13 It did not cover up what has 14 been done in the past during the review 15 process. I think that's most important. 16 Q. Doctor, once published, this 17 paper is available to the entire medical 18 and scientific community to review, 19 correct? 20 A. It was shown in PubMed and 21 other search engines. 22 Q. And, therefore, any 23 investigator desiring to read this 24 article will pull the article and see</p>	<p style="text-align: right;">Page 217</p> <p>1 a review process to determine whether 2 this paper is -- is anything that's 3 without conflict of interest. That's the 4 first thing. Because it can severely 5 affect the reviewer's mind. So when I 6 have time to look at the first submission 7 to Oncology, which was rejected, and then 8 later in the Reproductive Science, then 9 you can see there's a big difference in 10 Reproductive Science. 11 There's only single review. 12 And this is unusual in any review 13 process, only allow for only one review. 14 And further, I can just 15 reform the other opinions, that this 16 really complicated relationship between 17 the editorial office, authors, and I 18 don't know what's going on. I don't have 19 direct evidence. 20 But it's really -- I am so 21 intrigued how this paper can be 22 published. Omission -- this is junk 23 science totally without any biological 24 plausibility.</p>

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<p style="text-align: right;">Page 218</p> <p>1 DR. RESTAINO: I will</p> <p>2 strike -- move to strike the last</p> <p>3 statement as being unresponsive to</p> <p>4 the question.</p> <p>5 BY DR. RESTAINO:</p> <p>6 Q. Doctor, I just want to go</p> <p>7 over -- because in my mind I'm little a</p> <p>8 little bit confused about the chronology</p> <p>9 that we're dealing with. We discussed</p> <p>10 the grant that you have described in this</p> <p>11 paper and many other papers, the</p> <p>12 Department of Defense grant that you now</p> <p>13 say has expired, correct?</p> <p>14 A. The funding has expired.</p> <p>15 Q. If that began in 2014, is</p> <p>16 that -- is that what you testified?</p> <p>17 A. Which one?</p> <p>18 Q. Working with the grant?</p> <p>19 A. The grant?</p> <p>20 Q. Yes.</p> <p>21 A. The DOD grant.</p> <p>22 Q. Yes.</p> <p>23 A. I think it's clearly marked</p> <p>24 in my CV. I can give you the specific</p>	<p style="text-align: right;">Page 220</p> <p>1 from this DOD, from different things,</p> <p>2 from private foundation, for my own</p> <p>3 funding, to come out with this. So you</p> <p>4 really can't -- you can delineate which</p> <p>5 parts use this grant. There's no way</p> <p>6 that I can delineate that for you,</p> <p>7 neither could any scientist can opine</p> <p>8 you.</p> <p>9 Q. So now between 2011 and</p> <p>10 December 31st of 2018, the end of last</p> <p>11 year and that entire time, you did not</p> <p>12 consider conducting an experiment to look</p> <p>13 at the role of chronic inflammation and</p> <p>14 precursor cells associated with ovarian</p> <p>15 cancer; is that correct?</p> <p>16 A. For which period of time?</p> <p>17 Q. The entire period of time</p> <p>18 from December 31, 2018, back.</p> <p>19 A. Actually, chronic</p> <p>20 inflammation is one of the -- many of the</p> <p>21 hypothesis. So of course we have an</p> <p>22 interest to look at that. So our first</p> <p>23 paper publish in -- in by Ardighieri as</p> <p>24 you -- you know about. That is the one</p>
<p style="text-align: right;">Page 219</p> <p>1 date. Hold on a moment. It's very easy</p> <p>2 to find.</p> <p>3 So on Page 34. "Prevention</p> <p>4 of Ovarian High-Grade Serous Carcinoma by</p> <p>5 Elucidating its Early Changes,"</p> <p>6 W81XWH-11-2-0230. This is from</p> <p>7 October 1st, 2011.</p> <p>8 Q. Okay. So in 2011, now</p> <p>9 you've published a number of papers</p> <p>10 utilizing the histopathology slides that</p> <p>11 come under the umbrella of that grant,</p> <p>12 correct, you have several publications?</p> <p>13 A. I am not sure if it's a</p> <p>14 review paper or not reviews. I need to</p> <p>15 see which one you talk about.</p> <p>16 Q. Just talking in general.</p> <p>17 Did you publish papers based upon the</p> <p>18 work that you've done under the auspices</p> <p>19 of this grant?</p> <p>20 A. So as you know that the</p> <p>21 grant, we cannot only rely on one grant</p> <p>22 to publish something.</p> <p>23 Q. Okay.</p> <p>24 A. It is a network of grants,</p>	<p style="text-align: right;">Page 221</p> <p>1 that we publish as a best line, as a</p> <p>2 reference in the normal fallopian tube.</p> <p>3 What's the immune cell over there. Now</p> <p>4 this is a continuation of that.</p> <p>5 Q. I'm sorry. I'm sorry.</p> <p>6 During that time --</p> <p>7 A. Which time?</p> <p>8 Q. The time period of the last</p> <p>9 few years, working and publishing papers,</p> <p>10 did you -- you were aware of the -- the</p> <p>11 controversy regarding talc powder and</p> <p>12 ovarian cancer, correct?</p> <p>13 A. Between 2001 and --</p> <p>14 Q. Between 2011 and</p> <p>15 December 31st of 2018. You were aware of</p> <p>16 the controversy, correct?</p> <p>17 A. I heard from the news. But</p> <p>18 this is not my interest of research. I</p> <p>19 don't have any interest on that,</p> <p>20 because...</p> <p>21 Q. But after meeting with the</p> <p>22 attorneys for Johnson & Johnson it became</p> <p>23 an interest of yours and then you started</p> <p>24 your study a couple of weeks later; is</p>

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<p style="text-align: right;">Page 222</p> <p>1 that correct?</p> <p>2 MS. MILLER: Objection. I</p> <p>3 believe --</p> <p>4 THE WITNESS: I'm interested</p> <p>5 in chronic inflammation. Okay.</p> <p>6 Chronic inflammation, not talc.</p> <p>7 And in this study I did</p> <p>8 actually has nothing to do with</p> <p>9 talc. It's to do with chronic</p> <p>10 inflammation is present, absent or</p> <p>11 what happens associated with STIC</p> <p>12 and precursor signature. So this</p> <p>13 is not for the STIC litigation.</p> <p>14 It's part of a continuation of</p> <p>15 scientific curiosity. So it's not</p> <p>16 relevant.</p> <p>17 BY DR. RESTAINO:</p> <p>18 Q. In every publication dealing</p> <p>19 with chronic inflammation and ovarian</p> <p>20 cancer, prior to this interim report that</p> <p>21 we're now dealing with, you had</p> <p>22 co-authors working with you on every</p> <p>23 publication, correct?</p> <p>24 MS. MILLER: Objection.</p>	<p style="text-align: right;">Page 224</p> <p>1 And as I said, we have no</p> <p>2 idea yet, because I cannot predict</p> <p>3 what happen next year.</p> <p>4 BY DR. RESTAINO:</p> <p>5 Q. So when you write in your</p> <p>6 expert report that this paper is the</p> <p>7 final answer regarding the chronic</p> <p>8 inflammation in precursor cells, what are</p> <p>9 we to take from that?</p> <p>10 MS. MILLER: Objection. Can</p> <p>11 you point us to where he says</p> <p>12 that?</p> <p>13 BY DR. RESTAINO:</p> <p>14 Q. If you would look at the</p> <p>15 top -- first paragraph of Page 28 of his</p> <p>16 study report.</p> <p>17 MS. MILLER: You said when</p> <p>18 you write in your expert report.</p> <p>19 THE WITNESS: Expert</p> <p>20 reports?</p> <p>21 MS. MILLER: Now, you are</p> <p>22 talking about the study reports?</p> <p>23 DR. RESTAINO: The study</p> <p>24 reports.</p>
<p style="text-align: right;">Page 223</p> <p>1 THE WITNESS: I need to</p> <p>2 review the list, but I believe not</p> <p>3 all of them.</p> <p>4 BY DR. RESTAINO:</p> <p>5 Q. Have you published any paper</p> <p>6 that's not an editorial in which you</p> <p>7 did -- did not have co-authors?</p> <p>8 A. So you meant single author</p> <p>9 in what kind of paper?</p> <p>10 Q. Yes. You are the single</p> <p>11 author on this paper, correct?</p> <p>12 MS. MILLER: Objection. I</p> <p>13 think that mischaracterizes his</p> <p>14 testimony earlier today.</p> <p>15 THE WITNESS: We discussed</p> <p>16 that before. I said for the</p> <p>17 official publication we have not</p> <p>18 decided yet. I don't have time to</p> <p>19 think about what we want to come</p> <p>20 out with the research. It's a</p> <p>21 multiple research, or a single</p> <p>22 research, combined with molecular</p> <p>23 environment, molecular genetic,</p> <p>24 metabolomic, metagenetic.</p>	<p style="text-align: right;">Page 225</p> <p>1 MS. MILLER: Okay. That was</p> <p>2 not the question.</p> <p>3 Now, you said when you write</p> <p>4 in your expert report that this</p> <p>5 paper is the final answer, are you</p> <p>6 withdrawing that question?</p> <p>7 DR. RESTAINO: I'm</p> <p>8 withdrawing that question.</p> <p>9 BY DR. RESTAINO:</p> <p>10 Q. So when you write in your</p> <p>11 study report, "So the final answer from</p> <p>12 this study is that ovarian cancer</p> <p>13 precursor lesions are not associated with</p> <p>14 chronic inflammation, thus refuting the</p> <p>15 hypothesis that chronic inflammation is</p> <p>16 the cause of ovarian cancer," that that</p> <p>17 would not be an accurate statement at</p> <p>18 this time, correct?</p> <p>19 A. I'm sorry, I'm behind of</p> <p>20 you.</p> <p>21 Q. Okay.</p> <p>22 A. So where are you talking</p> <p>23 about, this page?</p> <p>24 Q. Study report, Page 28. Top</p>

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<p>1 paragraph of 28. 2 A. Okay. 3 Q. Okay. And so the final -- 4 the last sentence of that top paragraph 5 on Page 28 states, "So, the final answer 6 from this study is that ovarian cancer 7 precursor lesions are not associated with 8 chronic inflammation, thus refuting the 9 hypothesis that chronic inflammation is 10 the cause of ovarian cancer." 11 So, Doctor, you're making 12 that statement in this study report based 13 solely on your interim results, correct? 14 MS. MILLER: Objection. 15 THE WITNESS: This is the 16 opinion I gave in this interim 17 report. 18 BY DR. RESTAINO: 19 Q. Okay. Is that a litigation 20 opinion? 21 A. Litigation opinion. What do 22 you mean? 23 Q. I don't know, sir. You 24 described the opinions of Dr. Saed and</p>	<p>1 third line down you write, "I was asked 2 to review these litigation opinions and 3 to assess their scientific validity." 4 So, sir, I have to ask you, 5 what do you mean by litigation opinions? 6 A. Litigation opinions to me is 7 to review the material provided to me, 8 including deposition reports and their 9 opinions. 10 Q. Okay. So in reviewing the 11 deposition of Dr. Saed, to review 12 Dr. Kane's report, Dr. Saed's report, and 13 any other plaintiff expert you may have 14 reviewed, is it fair and equal to say 15 that your opinions that you're giving in 16 your expert report and today are 17 litigation opinions? 18 MS. MILLER: Objection. 19 THE WITNESS: It is my 20 research opinion. 21 BY DR. RESTAINO: 22 Q. Is it your research opinion 23 regarding the methodology that Dr. Kane 24 utilized?</p>
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<p>1 Dr. Kane in your expert report as 2 litigation opinion. 3 What do you mean? 4 MS. MILLER: Objection. 5 THE WITNESS: I think that 6 study was paid at least by writing 7 by the company. 8 BY DR. RESTAINO: 9 Q. You think. What about 10 Dr. Kane, the gynecological pathologist, 11 why are her expert opinions litigation 12 opinions and yours are not? 13 A. Can you show me what I say 14 over that? 15 Q. Sure. Let's go now to the 16 expert report. 17 A. Okay. 18 Q. And if you go to your 19 page -- first page -- 20 A. First page. 21 Q. -- Introduction of Scope of 22 Report and Summary of Opinions. 23 Do you see that, sir? 24 Okay. And then your -- the</p>	<p>1 MS. MILLER: Objection. 2 THE WITNESS: Those are two 3 different questions. 4 BY DR. RESTAINO: 5 Q. Well, you have an opinion 6 regarding Dr. Kane's methodology, 7 correct? 8 A. Where did I say that? 9 Q. In your expert report. 10 A. Where? Where? I'm sorry. 11 Q. Oh, I'm sorry. Number 2 on 12 that page, Dr. Saed's experimental 13 results. 14 MS. MILLER: Are you talking 15 about -- 16 BY DR. RESTAINO: 17 Q. No, I'm sorry, Number 1. 18 "Dr. Saed's and Dr. Kane's opinions 19 related to biological plausibility of the 20 theory that talc powder use can cause 21 ovarian cancer or increase the risk of 22 ovarian cancer are not the product of 23 reliable methods and are contrary to 24 established scientific knowledge."</p>

<p style="text-align: right;">Page 230</p> <p>1 Doctor, what was Dr. Kane's 2 methodology that, in your opinion, is 3 unreliable? 4 A. You meant Dr. Saed and 5 Dr. Kane together, or do you want me to 6 separate? 7 Q. Let's separate. I want to 8 talk -- 9 A. Okay. All right. 10 Q. Dr. Kane's methodology, what 11 about it was flawed? 12 A. I -- my opinion is she 13 reached the conclusion by leaving many 14 holes in between without showing any 15 biological plausibility in the mechanism. 16 Can I see that one? 17 MS. MILLER: What do you 18 want? Dr. Kane's report? 19 THE WITNESS: Yeah, Dr. Kane 20 report. 21 MS. MILLER: You have to ask 22 them if they're okay with that. 23 THE WITNESS: Is that okay, 24 that I can have a better</p>	<p style="text-align: right;">Page 232</p> <p>1 memory on the flaws in her methodology? 2 MS. MILLER: That's actually 3 not what I said. I said may he 4 look at his discussion of 5 Dr. Kane's opinions without 6 looking at Dr. Kane's report. 7 BY DR. RESTAINO: 8 Q. What do you need to look at 9 to tell us what part of Dr. Kane's 10 methodology was flawed? 11 A. It would be helpful to -- 12 for me to review it. 13 Q. Review what, sir? Let me 14 strike that question. Let me ask you 15 this. 16 Did Dr. Kane conduct a 17 systematic review of the literature? 18 MS. MILLER: Objection. 19 THE WITNESS: That, I don't 20 know. 21 BY DR. RESTAINO: 22 Q. As you sit here today, what 23 do you believe that Dr. Kane was basing 24 her opinions upon?</p>
<p style="text-align: right;">Page 231</p> <p>1 discussion for that? 2 BY DR. RESTAINO: 3 Q. As you sit here today, can 4 you tell us, without looking at your 5 expert report, what are the flaws in what 6 Dr. Kane utilized as her methodology? 7 MS. MILLER: I'm going to 8 object to that, because as I 9 recall at the beginning of the 10 deposition, you said this was not 11 a memory test. 12 THE WITNESS: Correct. 13 MS. MILLER: I mean, he 14 addresses Dr. Kane in his report. 15 Is he allowed to turn to where he 16 addresses Dr. Kane -- 17 DR. RESTAINO: Not if he's 18 going to sit here with his finger 19 going over every word in his 20 report, because if so, we're going 21 off the record. 22 BY DR. RESTAINO: 23 Q. Doctor, do you need to look 24 at Dr. Kane's report to refresh your</p>	<p style="text-align: right;">Page 233</p> <p>1 MS. MILLER: Objection. 2 THE WITNESS: From based on 3 what I recalled, she did a 4 literature search. I think she's 5 a pathologist. 6 BY DR. RESTAINO: 7 Q. And pathologists don't know 8 how to do literature researches? 9 A. I say she did literature 10 search. 11 Q. As you did also, correct? 12 A. I'm not sure what does that 13 mean, the same. We may use different key 14 words and search engines. I don't know 15 what she searched. 16 Q. So you're speculating on her 17 methodology? 18 MS. MILLER: No, he's not 19 speculating. 20 THE WITNESS: No, no. 21 MS. MILLER: You're refusing 22 to give him the report. 23 THE WITNESS: Yeah. 24 MS. MILLER: He'd like to</p>

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<p style="text-align: right;">Page 234</p> <p>1 look at the report. He's not 2 speculating. You're pressing him 3 to answer without the report. 4 BY DR. RESTAINO: 5 Q. Do you need to see 6 Dr. Kane's report? 7 A. If you have one, that would 8 be great. 9 DR. RESTAINO: I don't even 10 know if we have one. 11 BY DR. RESTAINO: 12 Q. If you assume that she used 13 the same keywords, chronic inflammation, 14 ovarian cancer -- you're shaking your 15 head no. 16 A. No, I don't know what you -- 17 what you meant. Could you speak slowly. 18 MS. MILLER: Shall we go off 19 the record and get a copy of the 20 report? 21 DR. RESTAINO: Sure. 22 THE WITNESS: I think that's 23 the best way. 24 MS. MILLER: Okay. Let's go</p>	<p style="text-align: right;">Page 236</p> <p>1 In my report, Page 8, Number 2 3, Dr. Kane's opinions. And I should 3 tell you that the methodologies Dr. Kane 4 used has many, many flaws, just like 5 Dr. Saed. And their opinions, the flawed 6 opinions, share a lot. 7 So I can tell you Dr. Kane's 8 incorrect methodology unique to her 9 report first. Then we can go back to 10 Saed because they overlap. 11 Q. What is it about her 12 methodology that you find to be flawed? 13 A. Okay. Number 1, is showing 14 in the Page 8, she claimed the lymphatic 15 transport -- should I go over the 16 sentences? I can do that. 17 Q. No. That's her opinion, 18 isn't it? 19 A. Right. So I can show you. 20 Q. I'm asking you, as to her 21 methodology to get to her opinions, what 22 about her methodology was flawed? 23 MS. MILLER: Objection. 24 THE WITNESS: She reached</p>
<p style="text-align: right;">Page 235</p> <p>1 off. 2 THE VIDEOGRAPHER: The time 3 is 1:56 p.m. We're going off the 4 record. 5 (Short break.) 6 THE VIDEOGRAPHER: The time 7 is 2:09 p.m. We're back on the 8 record. 9 BY DR. RESTAINO: 10 Q. Doctor, during the break, 11 did you have a chance to review Dr. Sarah 12 Kane's expert report? 13 MS. MILLER: No, he didn't. 14 As soon as I got it printed, I 15 brought it in here. I don't think 16 he had a chance. I mean, we got 17 it printed, and I brought it. 18 BY DR. RESTAINO: 19 Q. Doctor, in your expert 20 report, can you show me where you 21 describe the flaws in Sarah Kane's 22 methodology? 23 A. Sure. I think that's a fair 24 question.</p>	<p style="text-align: right;">Page 237</p> <p>1 her conclusion, which is 2 incorrect, based on those reports. 3 But that's her misinterpretation 4 of the result. And there's many 5 holes in between that prevent her 6 to come to a conclusion. 7 For example, the lymphatic 8 transport, the similarity between 9 talc structure and asbestos, and 10 also she confused mesothelioma and 11 high grade serous carcinoma. And 12 that's based on her search. 13 And then she claimed that 14 the talc is causal for ovarian 15 cancer, in which the methodology 16 is totally flawed, and there is no 17 biological plausibility. 18 As an example, I think she 19 is a pathologist. She knows 20 what's the difference between 21 mesothelioma and high grade serous 22 carcinoma, and she claim that 23 based on her experience that these 24 two are very similar.</p>

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<p style="text-align: right;">Page 238</p> <p>1 But it's not. They are not. 2 Every well -- every trained, I'm 3 sorry, every trained 4 board-certified pathologist can 5 tell them apart. They are so 6 different, not only in morphology, 7 their pathogenesis and the 8 clinical outcome, they are 9 different. 10 That's one. I think that 11 she did not have a correct 12 methodology in that opinion. 13 The other one is the 14 lymphatic spread -- 15 BY DR. RESTAINO: 16 Q. Okay. Let's go over the 17 first one there. 18 A. Okay. Okay. All right. 19 Q. We'll get too far ahead of 20 ourselves. Okay? Regarding the -- or 21 you believe that she has a flawed opinion 22 regarding how the human body will react 23 to different stimulus. If the -- if the 24 talc is absorbed in the lymphatic system</p>	<p style="text-align: right;">Page 240</p> <p>1 A. It depends. It depends on 2 what kind of tissues you are talking 3 about and the concentration of the talc 4 powders. 5 Q. Therefore, not all body 6 tissues are going to respond the same to 7 an external stimulus, correct? 8 MR. LOCKE: Objection. 9 THE WITNESS: But if the 10 concentration is the same, the 11 patients respond in a similar way. 12 BY DR. RESTAINO: 13 Q. Okay. Have you heard of the 14 bacterium <i>Helicobacter pylori</i> or 15 <i>H. pylori</i>? 16 MS. MILLER: Objection. 17 THE WITNESS: Yes. 18 BY DR. RESTAINO: 19 Q. Yes. It's known to cause 20 stomach adenocarcinoma, correct? 21 A. It cause peptic ulcer and 22 chronic inflammation. 23 Q. And hepatic carcinoma, 24 correct?</p>
<p style="text-align: right;">Page 239</p> <p>1 and -- and goes throughout the body, 2 correct? 3 MS. MILLER: Objection. I 4 don't think that was what he said. 5 BY DR. RESTAINO: 6 Q. Well, to -- to read what 7 you -- to read what you say about 8 lymphatic transport. "If talc particles 9 can travel through the lymphatic channel 10 to the ovaries, they should be able to 11 reach other human body parts and tissues 12 as well, because the lymphatic system 13 runs throughout the body. There are no 14 reports showing that talc is associated 15 with other types of female (or male) 16 cancer like colon cancer, liver cancer, 17 stomach cancer, prostate cancer, and 18 pancreatic cancer (where lymphatic 19 circulation is active) just to name a 20 few." 21 Okay. Now, Doctor, is it 22 your expert opinion that all tissue in 23 the human body will react the same way to 24 the same stimulus?</p>	<p style="text-align: right;">Page 241</p> <p>1 A. That's everybody believe. 2 Q. Everybody -- in fact, IARC 3 lists <i>H. pylori</i> as a Class I carcinogen, 4 does it not? 5 MS. MILLER: Objection. 6 THE WITNESS: I don't have 7 the documents with me. 8 BY DR. RESTAINO: 9 Q. And <i>H. pylori</i> is -- it is 10 contracted typically orally, correct? 11 MS. MILLER: Objection. 12 THE WITNESS: I'm a 13 pathologist, and a cancer 14 biologist and not 15 gastroenterologist. 16 BY DR. RESTAINO: 17 Q. Does the <i>H. pylori</i> travel 18 through the mouth and esophagus to get to 19 the stomach? 20 A. I'm not a microbiologist 21 either. 22 Q. Okay. Does the -- are 23 the -- are you aware of any reports of 24 <i>H. pylori</i> causing tongue cancer?</p>

<p style="text-align: right;">Page 242</p> <p>1 A. Again, I'm not the H. pylori 2 specialist. 3 Q. Does it cause upper 4 esophageal cancer? 5 A. I'm a gynecology 6 pathologist. We only care about below 7 diaphragm. 8 Q. Okay. So you don't know if 9 those tissues react differently to that 10 external stimulus, correct? 11 A. It's outside my opinion. 12 Q. Certain strains of human 13 papilloma virus or HPV are generally 14 accepted to cause cervical, vaginal, 15 vulvar, penile and oropharyngeal cancer, 16 correct? 17 A. Can you show me the 18 evidence? 19 Q. Are you not aware of what 20 forms of cancer H. papilloma virus cause? 21 A. H. pylori? Not HPV, right? 22 Q. Human papilloma virus. 23 A. Okay. 24 Q. HPV.</p>	<p style="text-align: right;">Page 244</p> <p>1 question? 2 THE WITNESS: How is this 3 relevant to -- to my role as a 4 cancer biologist in this case? 5 BY DR. RESTAINO: 6 Q. You are offering an opinion 7 that Dr. Kane's opinion regarding 8 lymphatic transport is different and 9 you're using an example of why it doesn't 10 cause cancer or problems in other body 11 parts. There you are an expert; is that 12 correct? 13 MS. MILLER: Objection. 14 Argumentive. 15 THE WITNESS: The lymphatic 16 transport of talcum powder as 17 Dr. Kane opined in the -- the 18 lymphatic system and the lymph 19 node, this is not relevant to 20 tubal -- okay. STIC and precursor 21 signatures. 22 Because in the fallopian 23 tube there is no lymph nodes. 24 BY DR. RESTAINO:</p>
<p style="text-align: right;">Page 243</p> <p>1 A. HPV. I think you said 2 H. pylori or -- 3 Q. Okay. I'll strike the 4 question and I'll ask it over again. 5 Certain strains of human 6 papilloma virus, HPV, generally accepted 7 to cause cervical, vaginal, vulvar -- 8 vulvar, penile and oropharyngeal cancers, 9 correct? 10 A. I think it has been shown in 11 many articles. 12 Q. But they are not known to 13 cause cancers of the upper reproductive 14 tract, are they? 15 A. Upper reproductive, meaning 16 from which organs? 17 Q. As a pathologist, what do 18 you -- what organs do you classify as 19 being of the upper reproductive tract? 20 MS. MILLER: Objection. 21 BY DR. RESTAINO: 22 Q. I want to use the organs you 23 are most comfortable with, sir. 24 MS. MILLER: Is that a</p>	<p style="text-align: right;">Page 245</p> <p>1 Q. Doctor. 2 A. Yeah. 3 Q. In your critique of 4 Dr. Kane's opinions, it is true, is it 5 not, that different body tissues react 6 differently to different stimuli, 7 correct? The esophagus does not react to 8 H. pylori, the antrum of the stomach 9 does, correct? 10 A. There is no evidence to show 11 the esophageal cancer at this moment. 12 But I don't know whether it will be shown 13 in the future years. 14 Q. And you don't know whether 15 it's going to be shown in the future 16 years or whether talc is transported 17 through the lymphatic system to the 18 pelvic lymph nodes where it could cause a 19 problem, or are you aware of a 20 publication this week on talc migrating 21 to the pelvic lymph nodes? Are you aware 22 of that publication, sir? 23 MR. LOCKE: Objection. 24 MS. MILLER: Objection.</p>

<p style="text-align: right;">Page 246</p> <p>1 That was like seven different</p> <p>2 questions.</p> <p>3 THE WITNESS: I think I'm</p> <p>4 distracted by your different</p> <p>5 questions so --</p> <p>6 BY DR. RESTAINO:</p> <p>7 Q. I'll strike that --</p> <p>8 A. How is it relevant to -- to</p> <p>9 the -- to the Dr. Kane's opinion?</p> <p>10 Q. Okay. You don't understand</p> <p>11 it; is that right?</p> <p>12 A. I don't know how relevant</p> <p>13 those questions that is -- that I can</p> <p>14 help you to answer.</p> <p>15 Q. Okay. How about</p> <p>16 hepatitis C, that's a bloodborne</p> <p>17 pathogen, correct?</p> <p>18 A. Yes.</p> <p>19 Q. Gets in the blood. So</p> <p>20 therefore, by definition it goes</p> <p>21 throughout the entire human body,</p> <p>22 correct?</p> <p>23 A. Right.</p> <p>24 Q. And hepatitis C form --</p>	<p style="text-align: right;">Page 248</p> <p>1 about, you criticize Dr. Kane for talking</p> <p>2 about chemical similarities between</p> <p>3 asbestos and talc, correct?</p> <p>4 A. I talk about that.</p> <p>5 Q. Yes. Now, when you were</p> <p>6 taking, as a student way back when, you</p> <p>7 took organic chemistry, correct?</p> <p>8 A. I did not teach organic</p> <p>9 chemistry.</p> <p>10 Q. Did you take it as a</p> <p>11 student?</p> <p>12 A. Many, many years ago.</p> <p>13 Q. I understand. Now, when you</p> <p>14 were taking chemistry, did you study the</p> <p>15 structural composition of various</p> <p>16 components, various chemicals, minerals,</p> <p>17 whatever, when you were taking organic or</p> <p>18 inorganic chemistry, you studied the</p> <p>19 structure of those compounds, correct,</p> <p>20 even water, H₂O, did you study that</p> <p>21 analysis, that structure?</p> <p>22 MS. MILLER: Hey, can we try</p> <p>23 to stick to one question at a</p> <p>24 time?</p>
<p style="text-align: right;">Page 247</p> <p>1 causes what form of cancer?</p> <p>2 A. Liver cancer.</p> <p>3 Q. It goes through all the</p> <p>4 different organs to get to the liver,</p> <p>5 correct, but it doesn't cause cancer in</p> <p>6 those other organs, right?</p> <p>7 A. That's hepatitis C itself.</p> <p>8 Q. Yes.</p> <p>9 A. But it cannot be</p> <p>10 extrapolated to other agents. Every</p> <p>11 agent are different.</p> <p>12 Q. Okay. Like H. pylori only</p> <p>13 affects the stomach, right? It's</p> <p>14 spreading and each body tissue is acting</p> <p>15 differently.</p> <p>16 Let's go and talk about the</p> <p>17 chemical similarities --</p> <p>18 MS. MILLER: Is that a</p> <p>19 question?</p> <p>20 THE WITNESS: No, that is</p> <p>21 not a question.</p> <p>22 BY DR. RESTAINO:</p> <p>23 Q. No. I'm moving on to Page 9</p> <p>24 now of your expert report. You talk</p>	<p style="text-align: right;">Page 249</p> <p>1 DR. RESTAINO: Yes, I'm</p> <p>2 sorry.</p> <p>3 THE WITNESS: So --</p> <p>4 MS. MILLER: I know you were</p> <p>5 getting excited, but I don't know</p> <p>6 that we understand what the</p> <p>7 question is.</p> <p>8 THE WITNESS: You were</p> <p>9 asking about water. Okay. I can</p> <p>10 answer -- answer you any water</p> <p>11 questions, can I? I don't know</p> <p>12 what kind of question of water in</p> <p>13 the biophysics and bioengineering</p> <p>14 and biochemistry.</p> <p>15 BY DR. RESTAINO:</p> <p>16 Q. There's a structure to water</p> <p>17 of two hydrogen atoms and an oxygen atom,</p> <p>18 correct?</p> <p>19 A. Yes.</p> <p>20 Q. Okay. So you are looking</p> <p>21 at -- studying the chemistry of water,</p> <p>22 you're looking at the structure of it,</p> <p>23 correct?</p> <p>24 MS. MILLER: Objection.</p>

<p style="text-align: right;">Page 250</p> <p>1 I'm sorry.</p> <p>2 THE WITNESS: I cannot</p> <p>3 remember what I took, the content</p> <p>4 in my organic chemistry back to</p> <p>5 many, many years ago.</p> <p>6 BY DR. RESTAINO:</p> <p>7 Q. Doctor, is there a</p> <p>8 difference in your mind between the</p> <p>9 chemical structure of talc and asbestos</p> <p>10 or the structural structure?</p> <p>11 MS. MILLER: Objection.</p> <p>12 THE WITNESS: Structure of</p> <p>13 the --</p> <p>14 MS. MILLER: Structural</p> <p>15 structure?</p> <p>16 THE WITNESS: I'm not a</p> <p>17 mineralogist.</p> <p>18 BY DR. RESTAINO:</p> <p>19 Q. You are not a -- but you</p> <p>20 criticize Dr. Kane for saying that there</p> <p>21 were chemical similarities between</p> <p>22 asbestos and talc, correct?</p> <p>23 A. I use my general opinions to</p> <p>24 show that structural similarity. It</p>	<p style="text-align: right;">Page 252</p> <p>1 said, correct?</p> <p>2 MS. MILLER: Objection. Can</p> <p>3 you show him where Dr. Kane says</p> <p>4 that?</p> <p>5 THE WITNESS: Right. I need</p> <p>6 to have a close comparison. I'm</p> <p>7 not sure that's what Dr. Kane</p> <p>8 said.</p> <p>9 BY DR. RESTAINO:</p> <p>10 Q. Okay.</p> <p>11 A. Could you have that line</p> <p>12 of -- and we can compare.</p> <p>13 Q. In your report, don't you</p> <p>14 criticize on Page 5 of the report that --</p> <p>15 A. Page 5?</p> <p>16 Q. Your expert report. I</p> <p>17 believe it's Page 5, and that's where you</p> <p>18 write, "There are chemical similarities</p> <p>19 between asbestos and talc, and there are</p> <p>20 striking pathological similarities</p> <p>21 between invasive serous ovarian cancer</p> <p>22 and mesothelioma."</p> <p>23 And you criticize Dr. Kane</p> <p>24 for saying that there's chemical -- that</p>
<p style="text-align: right;">Page 251</p> <p>1 doesn't mean that they are the same,</p> <p>2 carry the same effect on human tissue.</p> <p>3 That's why I'm going to say very general</p> <p>4 things. Okay. You -- if you want to ask</p> <p>5 me what's the really difference, oxygen</p> <p>6 and the bindings, I'm not -- it's outside</p> <p>7 my expertise and my opinion.</p> <p>8 Q. It is your opinion, though,</p> <p>9 that both talc and asbestos have</p> <p>10 structural similarity to some degree.</p> <p>11 Talc is not asbestos; is that correct?</p> <p>12 MS. MILLER: Are you reading</p> <p>13 a sentence from here?</p> <p>14 DR. RESTAINO: It's middle</p> <p>15 of the large paragraph on Page 9</p> <p>16 of the report.</p> <p>17 THE WITNESS: Okay.</p> <p>18 BY DR. RESTAINO:</p> <p>19 Q. "Therefore, both" --</p> <p>20 "although both talc and asbestos have</p> <p>21 structural similarity to some degree."</p> <p>22 Do you see that, sir?</p> <p>23 A. Yes.</p> <p>24 Q. And that's what Dr. Kane</p>	<p style="text-align: right;">Page 253</p> <p>1 there aren't not chemical similarities,</p> <p>2 don't you?</p> <p>3 A. I'm sorry. I'm so confused.</p> <p>4 You're jumping 9 and 5 and which section</p> <p>5 are you talking about? We are talking</p> <p>6 about Dr. Kane's opinion or my report?</p> <p>7 MS. MILLER: I'm not seeing</p> <p>8 anything on Page 5 that you just</p> <p>9 read. Page 5 is Dr. Saed.</p> <p>10 THE WITNESS: Right.</p> <p>11 MS. MILLER: So I'm really</p> <p>12 confused.</p> <p>13 THE WITNESS: I cannot see</p> <p>14 the arguments.</p> <p>15 DR. RESTAINO: Okay. Give</p> <p>16 me one second then.</p> <p>17 MS. MILLER: On Page 8 he</p> <p>18 quotes Dr. --</p> <p>19 BY DR. RESTAINO:</p> <p>20 Q. On Page 9 of your expert</p> <p>21 report.</p> <p>22 A. Okay. Page 9.</p> <p>23 Q. Okay. You have in quotation</p> <p>24 marks, "Chemical similarities between</p>

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<p>1 asbestos and talc," do you not?</p> <p>2 Page 9 of your expert</p> <p>3 report.</p> <p>4 MS. MILLER: That's quoting</p> <p>5 Dr. Kane, who he quotes in full on</p> <p>6 Page 8.</p> <p>7 DR. RESTAINO: Yes. I want</p> <p>8 to get him to say on the record</p> <p>9 that's Dr. Kane's words.</p> <p>10 THE WITNESS: That's Page 8?</p> <p>11 BY DR. RESTAINO:</p> <p>12 Q. Page 9. You have a</p> <p>13 paragraph that's titled, "Chemical</p> <p>14 Similarities Between Asbestos and Talc,"</p> <p>15 correct?</p> <p>16 A. Yes.</p> <p>17 Q. And then you say, "This is</p> <p>18 incorrect."</p> <p>19 What -- do you see where I</p> <p>20 am?</p> <p>21 A. Yeah.</p> <p>22 Q. Okay. So my question, I was</p> <p>23 talking to you before about the chemical</p> <p>24 similarities, you state -- your opinion</p>	<p>1 no biological plausibility -- I mean, the</p> <p>2 methodologies and the techniques for</p> <p>3 confirming -- not confirming, I'm sorry,</p> <p>4 strike that out -- to support the</p> <p>5 evidence that something is A or B or C.</p> <p>6 So at the time, meaning the technology,</p> <p>7 we don't have that yet.</p> <p>8 Q. So is it your opinion</p> <p>9 sitting here today, that it's no longer a</p> <p>10 valid scientific question to look at and</p> <p>11 see whether two compounds are analogous</p> <p>12 to one another in their effect on the</p> <p>13 body?</p> <p>14 MS. MILLER: Objection.</p> <p>15 THE WITNESS: Oh, this is</p> <p>16 really big questions. It's so</p> <p>17 general. There's many questions</p> <p>18 embedded in your question. Can</p> <p>19 you specify them as specific as</p> <p>20 possible?</p> <p>21 BY DR. RESTAINO:</p> <p>22 Q. Is it your opinion that it's</p> <p>23 no longer scientifically valid to</p> <p>24 consider analogy when looking at a causal</p>
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<p>1 is that there are structural</p> <p>2 similarities, correct?</p> <p>3 A. No. This is quote from</p> <p>4 Dr. Kane. I did not say that.</p> <p>5 Q. You write the next sentence,</p> <p>6 "Structural similarity of chemical</p> <p>7 compounds does not mean they have the</p> <p>8 same function or effects."</p> <p>9 Correct?</p> <p>10 A. "This structural</p> <p>11 similarity," in the second line, is</p> <p>12 referring to Dr. Kane's quotes, "Chemical</p> <p>13 similarity between asbestos and talc."</p> <p>14 That's her opinion, not my opinion.</p> <p>15 Q. Now, what Dr. Kane in her</p> <p>16 report was -- are you familiar with the</p> <p>17 Bradford Hill viewpoint of analogy?</p> <p>18 A. Could you show me the</p> <p>19 Bradford Hill?</p> <p>20 Q. Do you not know -- you are</p> <p>21 not aware of using analogy to determine</p> <p>22 causation?</p> <p>23 A. But that's back to 1965 when</p> <p>24 the science is really arcane and there is</p>	<p>1 question?</p> <p>2 MS. MILLER: Objection.</p> <p>3 THE WITNESS: It depends.</p> <p>4 BY DR. RESTAINO:</p> <p>5 Q. Okay. So Dr. Kane, when</p> <p>6 she's looking at talc and asbestos and</p> <p>7 making an analogy with them, is that an</p> <p>8 improper methodology for her to employ?</p> <p>9 MS. MILLER: Objection.</p> <p>10 THE WITNESS: It's incorrect</p> <p>11 methodology in this specific case,</p> <p>12 because asbestos is different from</p> <p>13 talc.</p> <p>14 BY DR. RESTAINO:</p> <p>15 Q. Have you asked any</p> <p>16 representative of Johnson & Johnson to</p> <p>17 provide you with any documentation they</p> <p>18 have on the similarity between talc and</p> <p>19 asbestos?</p> <p>20 MS. MILLER: Objection.</p> <p>21 THE WITNESS: I do not</p> <p>22 recall.</p> <p>23 BY DR. RESTAINO:</p> <p>24 Q. Did anyone from Johnson &</p>

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<p style="text-align: right;">Page 258</p> <p>1 Johnson provide you with any 2 documentation that they have on the 3 similarity between talcum powder and 4 asbestos? 5 MS. MILLER: Objection. 6 Lacks foundation. 7 THE WITNESS: This is not 8 relevant to my reason to be here 9 today. I'm here to testify 10 biological plausibility and 11 molecular mechanism together with 12 gynecology and pathology to 13 determine there's no biological 14 plausibility. Everything is not 15 credible science and the full 16 technology in this case. Period. 17 DR. RESTAINO: Move to 18 strike as unresponsive. 19 BY DR. RESTAINO: 20 Q. Did anyone from Johnson & 21 Johnson provide you with any 22 documentation they may have on the 23 similarity between talc and asbestos? 24 A. I think I already answered</p>	<p style="text-align: right;">Page 260</p> <p>1 MS. MILLER: Objection. 2 MR. LOCKE: Objection. 3 MR. MIZGALA: Objection. 4 MS. MILLER: Three 5 objections at once. I think they 6 call that a jinx. Kids. I don't 7 know if they still do that. 8 THE WITNESS: I don't know. 9 MS. MILLER: In my day they 10 called it a jinx. 11 BY DR. RESTAINO: 12 Q. Had you -- have you reviewed 13 the deposition of any Johnson & Johnson 14 mineralogist? 15 MS. MILLER: Objection. As 16 I said, anything that he has 17 reviewed would be on his list, 18 so... 19 BY DR. RESTAINO: 20 Q. Have you reviewed any -- 21 A. As I said, I reviewed 22 whatever had been provided. 23 Q. So, Doctor, when you are 24 approaching this now from your area of</p>
<p style="text-align: right;">Page 259</p> <p>1 your question. This is not relevant to 2 my position here. 3 Q. It's a yes or no question, 4 Doctor. Did anyone give you any 5 documentation that Johnson & Johnson may 6 have on the similarities between talc and 7 asbestos? 8 MS. MILLER: Same objection. 9 MS. SHARKO: Mr. Restaino, I 10 don't believe that any company 11 documents were supplied to 12 Dr. Shih if that is helpful. 13 DR. RESTAINO: I'll proceed 14 with your representation. 15 THE WITNESS: I don't know 16 that. Yeah. 17 MS. MILLER: Anything that 18 we provided him would be on his 19 reliance list, which you have. 20 BY DR. RESTAINO: 21 Q. Do you understand that 22 Johnson & Johnson has admitted that 23 asbestos has been in their talcum powder 24 products in the past?</p>	<p style="text-align: right;">Page 261</p> <p>1 expertise, as is Dr. Kane, is there a 2 difference between disagreeing with her 3 methodology and disagreeing with her 4 conclusions? 5 MS. MILLER: Objection. 6 THE WITNESS: Her 7 methodology is flawed, and her 8 conclusion is coming from nowhere. 9 BY DR. RESTAINO: 10 Q. Where in your expert report 11 does it discuss her methodology and why 12 it's flawed? 13 A. You mean Dr. Kane 14 specifically, right? 15 Q. Yes. 16 A. So as we discussed, there 17 are many thing that overlap with 18 Dr. Saed. So I would start from the -- 19 really the beginning. 20 Number one -- can I have the 21 report so I can refer to the figures 22 tables, Dr. Kane's? Or you don't need 23 that? 24 Q. No, the question is where in</p>

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<p style="text-align: right;">Page 262</p> <p>1 your expert report do you discuss her 2 methodology. 3 A. In -- okay. Page 8 and 4 Page 9 specifically, but there are also 5 overlap opinions against her in other 6 pages, like Page 5 and I believe on 7 Page 4, 5 -- I should say Page 4, 5, 6, 8 7, 8 and 9. 9 Q. What I see on each of them, 10 Doctor, is, in fact, for example, if you 11 go to Page 8, you have a Number 3, 12 Dr. Kane's opinions, correct? 13 A. Right. 14 Q. Where is your description of 15 how she got to those opinions which in 16 your opinion is flawed? 17 MS. MILLER: Objection -- 18 BY DR. RESTAINO: 19 Q. Where is -- I'm sorry. 20 Where is the description of her 21 methodology? 22 MS. MILLER: -- methodology. 23 Could we start over because that 24 is confusing. That was different</p>	<p style="text-align: right;">Page 264</p> <p>1 that the literatures I reviews, 2 and based on my credential, as you 3 can see my CV, and I review so 4 many papers, publish so many 5 papers, and with more than 32,000 6 citations, that's my expertise, 7 and I can judge as an authority in 8 ovarian cancer biology field that 9 her methodology is flawed. 10 And I already expressed my 11 concern in -- in this report. 12 BY DR. RESTAINO: 13 Q. Doctor, other than 14 disagreeing with her opinions, where in 15 your expert report do you describe what 16 methodology Dr. Kane used and why that 17 methodology is flawed? 18 MS. MILLER: Objection. 19 THE WITNESS: Her 20 methodology is based on the 21 literature she reviewed, and the 22 jump into the conclusion. But 23 there is many things that should 24 not prevent this jumping style</p>
<p style="text-align: right;">Page 263</p> <p>1 questions. 2 What is your question? 3 THE WITNESS: So it 4 should -- 5 BY DR. RESTAINO: 6 Q. Listed here is Dr. Kane's 7 opinions. Where is your description in 8 your expert report of the -- of the 9 methodology employed and why in your 10 opinion it was flawed? 11 MS. MILLER: Objection. 12 THE WITNESS: She had -- she 13 had several opinions like Dr. Saed 14 for example. Like ROS, reactive 15 oxygen trace -- 16 BY DR. RESTAINO: 17 Q. I'm going to move to strike. 18 Doctor, I understand, sir, 19 respectfully, I understand that you 20 disagree with her opinions. I'm asking, 21 where is your analysis of the method she 22 employed to get to her opinion. 23 MS. MILLER: Objection. 24 THE WITNESS: So I would say</p>	<p style="text-align: right;">Page 265</p> <p>1 conclusion. 2 So her conclusion is based 3 on no credible science and the 4 cogent evidence at all. So her 5 entire methodology she used is 6 wrong, because you jump around. 7 BY DR. RESTAINO: 8 Q. What methodology did she 9 use? 10 MS. MILLER: Objection. 11 THE WITNESS: The 12 methodology is like -- okay. So 13 this is the difference between 14 Dr. Kane and me. So it's very 15 difficult to prove negative. 16 So if this is a case Dr. -- 17 Dr. Kane and -- or Dr. Saed 18 propose that talcum powder can 19 cause ovarian cancer, you need to 20 show evidence. 21 So again, this is very 22 important. Science is evidence 23 driven. Evidence is held -- 24 BY DR. RESTAINO:</p>

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<p style="text-align: right;">Page 266</p> <p>1 Q. Doctor, with all due 2 respect, sir. I'm going to move to 3 strike. 4 MS. MILLER: Well, you asked 5 what methodology she used and he 6 was trying to explain that. 7 THE WITNESS: Yeah, that's 8 my -- that's my -- 9 MS. MILLER: I think that 10 actually he was answering your 11 question fairly. 12 THE WITNESS: Right. So 13 that's my -- my methodology. 14 MS. MILLER: He's trying to 15 explain the difference between his 16 methodology and her methodology. 17 THE WITNESS: Right. My 18 methodology is different from her 19 role. Her role is to demonstrate 20 the evidence positive. Okay. My 21 methodology, I cannot find any 22 positive credible science, cogent 23 evidence that can support the 24 biological mechanism of talc can</p>	<p style="text-align: right;">Page 268</p> <p>1 induce ovarian cancer. 2 Is that correct? That's 3 what you just said. 4 A. Yes, I did. 5 Q. Okay. Now, you are the -- 6 you are -- is it your position that the 7 Kimmel Center, is that you are the 8 director or co-director? 9 A. I'm co-director. 10 Q. You are the director? 11 A. Co-director. 12 Q. Co-director. I'm sorry, 13 sir. 14 A. Of breast and ovarian cancer 15 program. 16 Q. Okay. 17 A. Okay. 18 DR. RESTAINO: I'd like to 19 have marked as -- it's already 20 marked. 21 (Document marked for 22 identification as Exhibit 23 Shih-8.) 24 BY DR. RESTAINO:</p>
<p style="text-align: right;">Page 267</p> <p>1 induce ovarian cancer. So her 2 methodology, I -- totally is 3 wrong, okay, because she cannot 4 prove that, or she cannot provide 5 evidence for biological 6 plausibility. 7 BY DR. RESTAINO: 8 Q. Doctor, is there -- it is 9 your opinion, is it not, that there is no 10 evidence that talcum powder causes 11 ovarian cancer, correct? 12 MS. MILLER: Objection. Can 13 you point to where he said that? 14 BY DR. RESTAINO: 15 Q. Is that your opinion, 16 Doctor? 17 A. Do you know where -- where 18 is in the -- in my reports? Could you 19 show me line and the page? 20 Q. Well, first in your 21 testimony today, you said my methodology, 22 I cannot find any positive credible 23 science, cogent evidence, that support 24 the biological mechanism of talc can</p>	<p style="text-align: right;">Page 269</p> <p>1 Q. Exhibit 8, a copy of the 2 website from the Sidney Kimmel 3 Comprehensive Cancer Center. 4 Do you see that, sir? 5 Do you see at the top it 6 says Johns Hopkins University, Sidney 7 Kimmel Comprehensive Cancer Center, 8 correct? 9 A. Yes. 10 Q. And on the bottom of that 11 page, above age, it says, "Ovarian cancer 12 risk factors." 13 Do you see that, sir? 14 A. Can I take a minute to see 15 what's this about, because this is the 16 first time I ever see. 17 Q. You don't know what her own 18 website says -- states? 19 A. No, we -- I do not maintain 20 a website. I do research. 21 Q. Okay. Well, if you turn to 22 the bottom of the second page, do you see 23 where they list there, talcum powder and 24 asbestos?</p>

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<p style="text-align: right;">Page 270</p> <p>1 A. Where?</p> <p>2 Q. Page two at the bottom,</p> <p>3 talcum powder and asbestos.</p> <p>4 Do you see that, sir?</p> <p>5 A. "Habitual use of talcum</p> <p>6 powder on the genital area may" -- "may</p> <p>7 increase the risk of ovarian cancer, but</p> <p>8 the evidence is not strong."</p> <p>9 Q. But there's evidence. You</p> <p>10 just stated that there was no evidence.</p> <p>11 Your website says the evidence is not</p> <p>12 strong?</p> <p>13 MS. MILLER: That misstates</p> <p>14 his testimony. And you read his</p> <p>15 testimony. His evidence was about</p> <p>16 biological plausibility. I mean,</p> <p>17 this is the second time you're</p> <p>18 misstating his testimony.</p> <p>19 BY DR. RESTAINO:</p> <p>20 Q. Do you agree, Doctor, that</p> <p>21 there is evidence linking talcum powder</p> <p>22 with ovarian cancer?</p> <p>23 MS. MILLER: Objection.</p> <p>24 THE WITNESS: There is no</p>	<p style="text-align: right;">Page 272</p> <p>1 review everyone? Or what?</p> <p>2 MS. MILLER: I don't</p> <p>3 understand the question.</p> <p>4 THE WITNESS: I don't</p> <p>5 understand. Yeah, I can't</p> <p>6 understand.</p> <p>7 BY DR. RESTAINO:</p> <p>8 Q. In your review to make the</p> <p>9 determination that you do not find any</p> <p>10 evidence -- "I did not find any evidence</p> <p>11 molecular, biological, pathological, or</p> <p>12 epidemiological in nature that supports</p> <p>13 the conclusion that talc can cause or</p> <p>14 increase risk of ovarian cancer."</p> <p>15 Now do you understand what I</p> <p>16 mean by epidemiological evidence?</p> <p>17 A. Could you show me where --</p> <p>18 Q. Your Opinion Number 3. Take</p> <p>19 a look at your expert report. First</p> <p>20 page. Opinion Number 3.</p> <p>21 A. Which?</p> <p>22 Q. Number 3, "Based on the</p> <p>23 recent research findings as published, I</p> <p>24 did not find any evidence" --</p>
<p style="text-align: right;">Page 271</p> <p>1 credible science and cogent</p> <p>2 evidence to support the biological</p> <p>3 plausibility of talcum powder can</p> <p>4 induce ovarian cancer.</p> <p>5 BY DR. RESTAINO:</p> <p>6 Q. Why would it not -- why</p> <p>7 would it say that on the website if there</p> <p>8 was no biological plausible evidence?</p> <p>9 A. When you see this, it say</p> <p>10 "may increase," okay. Then, "The</p> <p>11 evidence is not strong," but this is --</p> <p>12 this is not the word that we use here.</p> <p>13 And also you can say -- you can see in</p> <p>14 the following sentence, okay -- from my</p> <p>15 view, this is totally hypothetical.</p> <p>16 There's no biological evidence to support</p> <p>17 biological plausibility and the mechanism</p> <p>18 at all.</p> <p>19 Q. And you're looking at the</p> <p>20 epidemiological evidence also, correct?</p> <p>21 MS. MILLER: Objection.</p> <p>22 What do you mean by that?</p> <p>23 THE WITNESS: So review,</p> <p>24 what do you mean I review? I</p>	<p style="text-align: right;">Page 273</p> <p>1 A. Hold on. Hold on. I do not</p> <p>2 see that. Page 3?</p> <p>3 Q. No, first page.</p> <p>4 A. First page.</p> <p>5 Q. Opinion Number 3.</p> <p>6 A. Okay.</p> <p>7 Q. "Based on the recent</p> <p>8 research findings as published, I did not</p> <p>9 find any evidence -- molecular,</p> <p>10 biological, pathological or</p> <p>11 epidemiological in nature -- that</p> <p>12 supports the conclusion that talc can</p> <p>13 cause or increase the risk of ovarian</p> <p>14 cancer."</p> <p>15 Did I read that correctly?</p> <p>16 A. This has been written in my</p> <p>17 report.</p> <p>18 Q. Yes. Now, in the website</p> <p>19 for Sidney Kimmel Cancer Center, it</p> <p>20 states that there is evidence, although</p> <p>21 it's not strong, correct?</p> <p>22 MS. MILLER: Objection.</p> <p>23 That misstates what the website</p> <p>24 says.</p>

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<p style="text-align: right;">Page 274</p> <p>1 THE WITNESS: I don't know 2 who wrote this. This is not from 3 me. So I cannot comment on that. 4 BY DR. RESTAINO: 5 Q. Okay. As part of your work 6 to -- for your opinions in your expert 7 report, you looked at the epidemiology of 8 chronic inflammation and the development 9 of cancer? 10 MS. MILLER: Objection. 11 THE WITNESS: Again, I'm not 12 an epidemiologist. But I review, 13 quickly scan several articles in 14 epidemiology field -- 15 BY DR. RESTAINO: 16 Q. Okay. Including -- 17 A. -- to come to my conclusion, 18 not based on single, not based on single 19 individual reports. 20 Q. Doctor, before we move on to 21 this study, I want to discuss with you 22 your Opinion Number 3 on the first page 23 of your report. 24 A. Can you read it? Are we on</p>	<p style="text-align: right;">Page 276</p> <p>1 Q. Doctor, I just handed you a 2 paper by Trabert, T-R-A-B-E-R-T. 3 MS. MILLER: No, it's fine. 4 I have that online. I think I 5 have the same study. 6 BY DR. RESTAINO: 7 Q. The title of it is 8 "Prediagnostic Serum Levels of 9 Inflammation Markers and Risk of Ovarian 10 Cancer in the Prostate, Lung, Colorectal 11 and Ovarian Cancer (PLCO) Screening 12 Trial." 13 Did I read that correctly? 14 A. That's the title. 15 Q. Yes. And this study is not 16 referenced in your expert report, is it? 17 A. Yes, it's not listed. 18 Q. And this paper was published 19 in Gynecologic Oncology in 2014, correct? 20 The citation is right above the title. 21 Do you see that, sir? 22 A. Yes, I do. 23 Q. Do you recognize that as 24 being Gynecological Oncology, 2014,</p>
<p style="text-align: right;">Page 275</p> <p>1 the same page? 2 Q. Opinion Number 3 on the 3 first page, the same one we were just 4 looking at. 5 Did you write that opinion? 6 A. You mean starting from, 7 "Based on recent research findings"? 8 Q. Yes. 9 A. "As published." 10 Q. Did you write that? 11 A. Yes. 12 Q. No one else helped you with 13 any part of your report? 14 A. I don't think so. 15 Q. You don't think so, or you 16 know so? 17 A. There's nobody to help me. 18 Q. Nobody else? 19 A. Yes. 20 Q. Okay. 21 (Document marked for 22 identification as Exhibit 23 Shih-10.) 24 BY DR. RESTAINO:</p>	<p style="text-align: right;">Page 277</p> <p>1 November, correct? 2 A. Yes. 135, Page 297, yes. 3 Q. Okay. Now, in the title 4 we're dealing with inflammation markers 5 and the risk of ovarian cancer, correct? 6 A. That was written down in the 7 title. 8 Q. Okay. Now, if one was 9 conducting -- such as yourself, 10 conducting a review of the literature 11 after 2014 using keywords "inflammation" 12 and "ovarian cancer," one should find 13 this article, correct? 14 A. That's a hypothetical. How 15 can you know that we have come up with 16 this one? 17 Q. Okay. When you conducted 18 your literature search utilizing the 19 keywords ovarian cancer and inflammation, 20 did you find this article? 21 A. I cannot recall. But I 22 did -- I pull out those references, the 23 most relevant, and provide biological 24 plausibility or mechanism. Then I will</p>

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<p style="text-align: right;">Page 278</p> <p>1 take a look and cite it. But this one 2 is -- it's junk science. It did not tell 3 you anything about biological 4 plausibility. 5 Q. What are you referring to? 6 A. This paper. 7 Q. How do you know that if you 8 haven't even looked at the paper? 9 A. Now I remember. I saw this 10 paper. 11 MS. MILLER: This paper is 12 on his supplemental reliance list 13 produced yesterday, sir. 14 THE WITNESS: Yeah, I 15 remember that I saw this. 16 MS. MILLER: I don't know if 17 you noticed. 18 BY DR. RESTAINO: 19 Q. So you remember -- so you 20 have reviewed this? 21 MS. MILLER: He never said 22 he hadn't. 23 BY DR. RESTAINO: 24 Q. Okay. Now --</p>	<p style="text-align: right;">Page 280</p> <p>1 Q. And none of these 2 individuals are experts in the talcum 3 powder litigation, correct? 4 A. I don't know. 5 Q. Do you know if -- if members 6 of the NCI are allowed to work in legal 7 controversies such as this? 8 A. This is beyond my expert. 9 Q. Okay. Fair enough. Fair 10 enough. 11 Turn to the introduction on 12 Page 1 which is the next -- or it's 13 actually Page 2, the next page. 14 Introduction. 15 Do you see that, sir? 16 A. Yes. 17 Q. Very first paragraph under 18 the word introduction states, 19 "Epidemiological evidence implicates 20 chronic inflammation as a central 21 mechanism in the pathogenesis of ovarian 22 cancer, the most lethal gynecologic 23 cancer among women in the United States. 24 Reference 1."</p>
<p style="text-align: right;">Page 279</p> <p>1 MS. MILLER: If you look at 2 his supplemental reliance list, it 3 was listed on there. 4 BY DR. RESTAINO: 5 Q. Okay. Now, sir, each of 6 these authors are with the National 7 Cancer Institute, correct? 8 A. I need to double-check. 9 Division of Cancer 10 Epidemiology, National -- NCI -- NIH, HPV 11 Immunology, Frederick National Laboratory 12 for Cancer Research, National Cancer 13 Institute, National Institute of Health 14 Department of Health Human Service, 15 Frederick, Division of Cancer Prevention, 16 National Cancer Institute, National 17 Institute of Health. 18 MS. MILLER: If you're going 19 to read to yourself, you need to 20 read to yourself. 21 THE WITNESS: Correct. You 22 are totally correct. They are for 23 NIH. 24 BY DR. RESTAINO:</p>	<p style="text-align: right;">Page 281</p> <p>1 Did I read that correctly? 2 A. That's the words in this 3 paper. 4 Q. I'm sorry? 5 A. That's the words put in the 6 paper. 7 Q. The wart? 8 A. The words. The words. 9 MS. MILLER: Words. 10 BY DR. RESTAINO: 11 Q. Words, okay. In the paper, 12 correct? 13 A. Yes. It is words. Just 14 words. 15 Q. Okay. Now, if you turn and 16 you look at reference Number 1, in the 17 back, on Page 9, are you there, sir? 18 A. Yes. 19 Q. The authors from the 20 National Cancer Institute are referencing 21 the Centers For Disease Control and 22 Prevention, ovarian cancer statistics. 23 2010, correct? 24 A. That's what was cited.</p>

<p style="text-align: right;">Page 282</p> <p>1 Q. Okay. And the Centers For 2 Disease Control and Prevention, they are 3 known as the CDC, would you agree? 4 A. Agree. 5 Q. So we've got authors from 6 the NCI referencing the CDC, correct? 7 A. As it appears. 8 Q. Okay. Now I want to break 9 down that first sentence for you, sir. 10 It has two parts. 11 First part is, 12 "Epidemiologic evidence implicates 13 chronic inflammation as a central 14 mechanism in the pathogenesis of ovarian 15 cancer." 16 Do you see that -- that 17 verbiage, sir? 18 A. As it has been written in 19 this way. 20 Q. Okay. Do you have any 21 objective evidence to contradict that 22 statement? 23 MS. MILLER: Objection. 24 THE WITNESS: Your statement</p>	<p style="text-align: right;">Page 284</p> <p>1 type of ovarian cancer they are 2 talking about in this paper. High 3 grade serous, low grade serous, 4 endometriosis, carcinoma, sarcoma, 5 I don't know. 6 So this one is too vague. 7 BY DR. RESTAINO: 8 Q. Do you think -- do you think 9 the researchers from the National Cancer 10 Institute know the difference? 11 MS. MILLER: Objection. 12 Calls for speculation. 13 DR. RESTAINO: I'll withdraw 14 it. 15 BY DR. RESTAINO: 16 Q. Doctor, can a reasonable 17 scientist agree with the statement, 18 "Epidemiologic evidence implicates 19 chronic inflammation as a central 20 mechanism in the pathogenesis of ovarian 21 cancer"? 22 MS. MILLER: Objection. 23 THE WITNESS: They -- no, 24 they should not. Because there is</p>
<p style="text-align: right;">Page 283</p> <p>1 or this statement, or -- 2 BY DR. RESTAINO: 3 Q. The statement "epidemiologic 4 evidence implicates chronic inflammation 5 as a central mechanism in the 6 pathogenesis of ovarian cancer." 7 A. So this is the first 8 sentence you are referring to, right? 9 Q. Yes, sir. 10 A. Do you know how many 11 sentences in this article? 12 Q. Sir, I'm just asking if you 13 agree with these authors from the NCI 14 when they write, "Epidemiologic evidence 15 implicates chronic inflammation as a 16 central mechanism in the pathogenesis of 17 ovarian cancer." 18 Do you disagree with that? 19 MS. MILLER: Objection. 20 THE WITNESS: I don't know 21 any credible science and cogent 22 evidence to show chronic 23 inflammation can cause ovarian 24 cancer. And I don't know which</p>	<p style="text-align: right;">Page 285</p> <p>1 no credible science, cogent 2 evidence to support biological 3 plausibility. If it's 4 epidemiology, it's epidemiology. 5 If it's an association study, 6 association is not causal. So I 7 think that's a key point. 8 Association. It's just 9 association. So many things can 10 be associated with something. 11 BY DR. RESTAINO: 12 Q. So, Doctor, is it your 13 opinion that these authors from the 14 National Cancer Institute publishing in 15 Gynecological Oncology are not reasonable 16 scientists? 17 MS. MILLER: Objection. 18 THE WITNESS: I view the 19 science not by the authors or 20 their institutions or the journal 21 they published. I am a scientist. 22 I think I am a good scientist. 23 Probably one of the best 24 scientists in gynecology fields,</p>

<p style="text-align: right;">Page 286</p> <p>1 okay.</p> <p>2 So that's why we did.</p> <p>3 That's why we teach students,</p> <p>4 based on the science. If it's</p> <p>5 good science, it's good science.</p> <p>6 If it's bad science, it just don't</p> <p>7 support at all. Don't even create</p> <p>8 any anything to --</p> <p>9 DR. RESTAINO: I move to</p> <p>10 strike as unresponsive.</p> <p>11 BY DR. RESTAINO:</p> <p>12 Q. Doctor, can a reasonable</p> <p>13 scientist agree with the scientists from</p> <p>14 the National Cancer Institute when they</p> <p>15 publish in Gynecologic Oncology and</p> <p>16 reference the CDC, is it reasonable for a</p> <p>17 scientist to rely upon that?</p> <p>18 MS. MILLER: Objection.</p> <p>19 MR. LOCKE: Objection.</p> <p>20 MS. MILLER: That is just</p> <p>21 objectionable in so many ways, I</p> <p>22 won't go into them. I don't want</p> <p>23 to get in trouble for too many</p> <p>24 speaking objections that Michelle</p>	<p style="text-align: right;">Page 288</p> <p>1 citation for this statement?</p> <p>2 DR. RESTAINO: Move to</p> <p>3 strike as unresponsive.</p> <p>4 BY DR. RESTAINO:</p> <p>5 Q. Doctor, from your knowledge</p> <p>6 as a pathologist, okay, just using that</p> <p>7 alone, rapid cell division increases the</p> <p>8 possibility for replication error, does</p> <p>9 it not?</p> <p>10 MS. MILLER: Objection.</p> <p>11 THE WITNESS: As a</p> <p>12 scientist, probably one of the</p> <p>13 best scientists in this field, I</p> <p>14 only trust the evidence, not based</p> <p>15 on whatever, whoever talk about</p> <p>16 this.</p> <p>17 I need to see the evidence.</p> <p>18 Where is the citation?</p> <p>19 BY DR. RESTAINO:</p> <p>20 Q. Have you -- have you ever</p> <p>21 seen evidence that chronic inflammation</p> <p>22 induces rapid cell division? That's</p> <p>23 common pathological physiology, is it</p> <p>24 not, sir?</p>
<p style="text-align: right;">Page 287</p> <p>1 doesn't like.</p> <p>2 THE WITNESS: I think my</p> <p>3 answer can apply to this question</p> <p>4 too. So I don't need to</p> <p>5 reiterate.</p> <p>6 BY DR. RESTAINO:</p> <p>7 Q. Okay. Let's look at the</p> <p>8 next sentence.</p> <p>9 A. Okay.</p> <p>10 Q. "Chronic inflammation can</p> <p>11 induce rapid cell division, increasing</p> <p>12 the possibility for replication error,</p> <p>13 ineffective DNA repair and subsequent</p> <p>14 mutation."</p> <p>15 Did I read that correctly?</p> <p>16 A. It has been written in this</p> <p>17 way.</p> <p>18 Q. Okay. And do you have any</p> <p>19 objective evidence to contradict the NCI</p> <p>20 researchers when they state that chronic</p> <p>21 inflammation can induce rapid cell</p> <p>22 division?</p> <p>23 MS. MILLER: Objection.</p> <p>24 THE WITNESS: Where is the</p>	<p style="text-align: right;">Page 289</p> <p>1 A. It depends on the --</p> <p>2 MS. MILLER: Objection.</p> <p>3 Hold on, Dr. Shih, let me object.</p> <p>4 THE WITNESS: Okay. I'm</p> <p>5 sorry.</p> <p>6 MS. MILLER: There were two</p> <p>7 questions there. Which one do you</p> <p>8 want him to answer?</p> <p>9 THE WITNESS: Right.</p> <p>10 BY DR. RESTAINO:</p> <p>11 Q. Do you agree chronic</p> <p>12 inflammation can induce rapid cell</p> <p>13 division?</p> <p>14 A. That's too general. It</p> <p>15 depends on the tissue type, your severity</p> <p>16 of chronic inflammation, the patient's</p> <p>17 immunity, and also the defense mechanism</p> <p>18 and also circulation, ischemic status,</p> <p>19 and many things.</p> <p>20 Q. Can a reasonable scientist</p> <p>21 agree that chronic inflammation induces</p> <p>22 rapid cell division in carcinogenicity?</p> <p>23 A. No. I don't see any</p> <p>24 evidence for that though.</p>

<p style="text-align: right;">Page 290</p> <p>1 Q. Okay. Can a reasonable 2 scientist agree that rapid cell division 3 increases the possibility of replication 4 error? 5 MS. MILLER: Objection. 6 Agree with what? 7 DR. RESTAINO: Who it's 8 from -- 9 THE WITNESS: Who say that? 10 Who say that statement? Who are 11 the scientists and -- 12 BY DR. RESTAINO: 13 Q. The researchers from the 14 NCI. We just read it. I'll read it 15 again for you. Please keep this in your 16 mind, Doctor. 17 "Chronic inflammation can 18 induce rapid cell division increasing the 19 possibility for replication error, 20 ineffective DNA repair, and subsequent 21 mutations written by researchers from the 22 National Cancer Institute, published in 23 the peer reviewed publication Gynecologic 24 Oncology 2014."</p>	<p style="text-align: right;">Page 292</p> <p>1 too much to list to them all. 2 THE WITNESS: Which tissue? 3 Which cell you said? Different 4 scientist has a different -- 5 BY DR. RESTAINO: 6 Q. Doctor, do you agree, then, 7 that rapid cell division in the generic 8 sense increases the possibility for 9 replication error? 10 MS. MILLER: Objection. 11 THE WITNESS: I'm a 12 scientist, okay. Our research is 13 involving very similar in this 14 field. And we are the experts on 15 the endometrial repair and cancer 16 genetics. 17 So I can tell you as one -- 18 I am one of this authority in this 19 replication and DNA damage repair. 20 This question is making no 21 sense. 22 It depends on the context, 23 tissue, cell lines, and 24 methodology you used.</p>
<p style="text-align: right;">Page 291</p> <p>1 Doctor, can a reasonable 2 scientist agree with these scientists 3 from the NCI when they state that chronic 4 inflammation can induce rapid cell 5 division? 6 MS. MILLER: Objection. 7 THE WITNESS: There is no 8 credible science and cogent 9 evidence to show that chronic 10 inflammation, where two of those 11 things envelop into epithelial 12 cells, which is irrelevant to 13 ovarian cancer -- I mean, high 14 grade serous carcinoma. 15 DR. RESTAINO: I'm going to 16 move to strike. 17 BY DR. RESTAINO: 18 Q. Is it -- the question, 19 Doctor, is it reasonable for a reasonable 20 scientist to agree with these scientists 21 from the NCI? 22 MS. MILLER: Objection. 23 Asked and answered. Vague. Many 24 other things, but my head hurts</p>	<p style="text-align: right;">Page 293</p> <p>1 This question, I cannot 2 answer. Probably if you break up 3 into 20 specific questions, maybe 4 I can answer you individually. 5 BY DR. RESTAINO: 6 Q. Okay. Doctor, is limitless 7 replication potential one of the 8 hallmarks of carcinogenicity? 9 MS. MILLER: Objection. 10 THE WITNESS: So you are 11 talking about the cancer, what is 12 the feature of cancer? So you 13 said endless replication -- 14 MS. MILLER: Limitless. 15 BY DR. RESTAINO: 16 Q. Limitless. 17 A. Oh, limitless. 18 MS. MILLER: Like without 19 limits. 20 THE WITNESS: Okay. 21 Replication. Is like uncontrolled 22 proliferation. 23 BY DR. RESTAINO: 24 Q. Is that one of the hallmarks</p>

<p style="text-align: right;">Page 294</p> <p>1 of cancer?</p> <p>2 MS. MILLER: Objection.</p> <p>3 Vague.</p> <p>4 THE WITNESS: It's one of</p> <p>5 them is not sufficient for the</p> <p>6 cancer. But you said</p> <p>7 carcinogenicity, which is wrong.</p> <p>8 Carcinogenicity meaning</p> <p>9 initiation.</p> <p>10 So in the precursor lesion,</p> <p>11 which I'm the expert in the</p> <p>12 precursor of high grade serous</p> <p>13 carcinoma, which is p53 signature,</p> <p>14 and STIC. In the p53 signature,</p> <p>15 there is no proliferation at all.</p> <p>16 BY DR. RESTAINO:</p> <p>17 Q. Doctor, in what -- it is</p> <p>18 true, is it not, that another hallmark of</p> <p>19 cancer is self-sufficiency and growth</p> <p>20 signals, correct?</p> <p>21 MS. MILLER: Objection.</p> <p>22 THE WITNESS: In which</p> <p>23 context? And what kind of</p> <p>24 evidence that -- where does that</p>	<p style="text-align: right;">Page 296</p> <p>1 one, please show me.</p> <p>2 BY DR. RESTAINO:</p> <p>3 Q. Okay. How about tissue</p> <p>4 invasion and metastases, is that a</p> <p>5 hall -- are they a hallmark of cancer?</p> <p>6 MS. MILLER: Objection.</p> <p>7 THE WITNESS: It's one of</p> <p>8 the features.</p> <p>9 BY DR. RESTAINO:</p> <p>10 Q. Evading apoptosis, is that</p> <p>11 another feature or hallmark of cancer?</p> <p>12 MS. MILLER: Objection.</p> <p>13 THE WITNESS: It is -- okay.</p> <p>14 It's one of the features</p> <p>15 that someone proposed. But it</p> <p>16 depends on the tissue type. In</p> <p>17 ovarian cancer I did not show -- I</p> <p>18 did not see any cogent evidence to</p> <p>19 show that biological evidence that</p> <p>20 this occur in ovarian high-grade</p> <p>21 serous carcinoma. If it's HGSC,</p> <p>22 it's what we refer.</p> <p>23 But I would agree, this is</p> <p>24 in generic. But if you focus on a</p>
<p style="text-align: right;">Page 295</p> <p>1 statement come from?</p> <p>2 BY DR. RESTAINO:</p> <p>3 Q. You're not familiar with</p> <p>4 that statement? "Self-sufficiency and</p> <p>5 growth signals is a hallmark of cancer"?</p> <p>6 A. Can you show me the</p> <p>7 reference?</p> <p>8 Q. We'll get back to that in a</p> <p>9 moment.</p> <p>10 A. Please.</p> <p>11 Q. How about insensitivity to</p> <p>12 antigrowth signals? Is that a hallmark</p> <p>13 of cancer?</p> <p>14 A. What?</p> <p>15 MS. MILLER: Objection.</p> <p>16 BY DR. RESTAINO:</p> <p>17 Q. Insensitivity to antigrowth</p> <p>18 signals. Have you heard that phrase</p> <p>19 before?</p> <p>20 MS. MILLER: Objection.</p> <p>21 THE WITNESS: It depends on</p> <p>22 the cancer type. But in ovarian</p> <p>23 high grade carcinoma here, I don't</p> <p>24 see any evidence. If you have</p>	<p style="text-align: right;">Page 297</p> <p>1 specific type, you need -- one</p> <p>2 need to be careful.</p> <p>3 BY DR. RESTAINO:</p> <p>4 Q. Let's look again at the</p> <p>5 Trabert paper, sir. The very next</p> <p>6 sentence states, "Ovarian cancer has been</p> <p>7 linked to several events and conditions</p> <p>8 which are related to inflammation and</p> <p>9 repair, including incessant ovulation,</p> <p>10 endometriosis, exposure to talc and</p> <p>11 asbestos, and in some studies, pelvic</p> <p>12 inflammatory disease [Reviewed in [2]]."</p> <p>13 Did I read that correctly,</p> <p>14 sir?</p> <p>15 A. It is stemming from the</p> <p>16 review articles.</p> <p>17 Q. Okay. Do you agree with the</p> <p>18 statement, sir?</p> <p>19 MS. MILLER: Objection.</p> <p>20 THE WITNESS: I don't see</p> <p>21 any credible science and</p> <p>22 biological evidence to support</p> <p>23 this argument.</p> <p>24 And this, you show me the</p>

<p style="text-align: right;">Page 298</p> <p>1 good references. 2 BY DR. RESTAINO: 3 Q. Do you agree that incessant 4 ovulation has been linked to ovarian 5 cancer? 6 A. It has been proposed. 7 Q. Do you agree that 8 endometriosis has been epidemiologically 9 linked with ovarian cancer? 10 MS. MILLER: Objection. 11 THE WITNESS: Endometriosis, 12 there are different types. Only 13 certain type can do that, can 14 have -- increase very, very slight 15 risk. 16 BY DR. RESTAINO: 17 Q. So you're saying there's a 18 chance? 19 MS. MILLER: When you say -- 20 I'm confused. If you understand 21 his answer. When you say only 22 certain types, are you talking 23 about other than certain types of 24 endometriosis, or only certain</p>	<p style="text-align: right;">Page 300</p> <p>1 related to ovarian endometriotic 2 cysts, or so-called endometrioma, 3 so-called chocolate cyst. 4 So that is where the origin 5 of this clear cell endometrial 6 carcinoma, form this endometrioid 7 cyst. But the regular invasive 8 endometriosis and the superficial 9 endometriosis will not cause clear 10 cell and malignant carcinoma. Why 11 I know this? Because we just 12 publish one paper on this issue. 13 DR. RESTAINO: I'm going to 14 move to strike as unresponsive. 15 MS. MILLER: It was 16 completely responsive. You asked 17 him whether endometriosis was 18 related to endometrioid -- 19 THE WITNESS: Yeah. Right. 20 MS. MILLER -- whether 21 endometriosis was related to 22 ovarian cancer. And he's giving 23 you a full answer, because there 24 is no one entity called ovarian</p>
<p style="text-align: right;">Page 299</p> <p>1 types of ovarian cancer? 2 THE WITNESS: Oh, I'm sorry. 3 Look at this chart, okay. So this 4 is the origin of different types 5 of ovarian cancer. You can see 6 there is -- fallopian tube 7 epithelium is the origin of high 8 grade and low grade serous 9 carcinoma, we see here. 10 And endometriosis may be 11 related to endometrioid and clear 12 cell carcinoma. Actually, this is 13 very good evidence. 14 BY DR. RESTAINO: 15 Q. So these -- 16 MS. MILLER: Let him finish 17 his answer. 18 THE WITNESS: How do you 19 know what I'm going to say? I'm 20 sorry. I want to give you the 21 complete answer. 22 You see endometriosis, 23 especially the endometrioid type, 24 cancer and clear cells, they are</p>	<p style="text-align: right;">Page 301</p> <p>1 cancer. If he wants to talk about 2 the subtypes, that's a totally, 3 completely responsive answer. 4 THE WITNESS: Otherwise, 5 I -- 6 MS. MILLER: Otherwise your 7 question was misleading. 8 BY DR. RESTAINO: 9 Q. Doctor, these researchers 10 from the National Cancer Institute write 11 that endometriosis is linked with ovarian 12 cancer. Do you disagree or agree with 13 that? 14 A. Can you say that one more 15 time? Because now we are jumping 16 endometriosis to this. 17 Q. The authors here state -- 18 A. Yeah. 19 Q. -- "Ovarian cancer has been 20 linked to several events and conditions 21 which are related to inflammation and 22 repair" -- 23 A. Right. 24 Q. -- "including incessant</p>

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<p style="text-align: right;">Page 302</p> <p>1 ovulation." 2 A. Right. 3 Q. Endometriosis, do you agree 4 that endometriosis has been linked to 5 with inflammation and ovarian cancer? 6 MS. MILLER: Objection. 7 THE WITNESS: You said 8 linked to the inflammation, that I 9 don't know. 10 BY DR. RESTAINO: 11 Q. Okay. How about exposure to 12 talc and asbestos? 13 A. Definitely not. 14 Q. You disagree with that. 15 "And in some studies pelvic inflammatory 16 disease." 17 Do you agree with that? 18 MS. MILLER: Objection. 19 THE WITNESS: I did not say 20 I agree. 21 MS. MILLER: With what? 22 THE WITNESS: With what -- 23 and what -- what's your subjects? 24 BY DR. RESTAINO:</p>	<p style="text-align: right;">Page 304</p> <p>1 is 3:11 p.m. We are going off the 2 record. 3 (Short break.) 4 THE VIDEOGRAPHER: The time 5 is 3:21 p.m. We are back on the 6 record. 7 BY DR. RESTAINO: 8 Q. Welcome back, Doctor. 9 Now, Doctor, several times 10 today if I recall correctly, you've 11 stated that you are -- your publications 12 are frequently cited in the medical 13 literature; is that correct? 14 A. Frequently means -- do you 15 have a quantification? 16 Q. I -- I think you said, was 17 it 30,000 times? 18 A. 32,800. I don't know. I 19 cannot keep track on that. 20 Q. Okay. But it's about 30,000 21 or 32,000? 22 A. About. 23 Q. And that means that there is 24 a lot of publications that are -- that</p>
<p style="text-align: right;">Page 303</p> <p>1 Q. Do you need me to read the 2 sentence to you again? 3 A. No. No. 4 Q. Because I will. I'll read 5 it for as long as it takes the Number 1 6 pathologist in ovarian cancer to get it. 7 Ovarian cancer -- you 8 understand that, right? 9 MS. SHARKO: Wait, wait, 10 wait, Doctor. 11 MS. MILLER: Let's take a 12 break so you can relax. Let's 13 take a break so you can catch your 14 breath because you are kind of 15 shouting at the witness. 16 THE WITNESS: Right. Right. 17 MS. MILLER: Let's go off 18 the record. 19 THE VIDEOGRAPHER: Okay. Go 20 off? 21 I need confirmation from 22 both sides. 23 DR. RESTAINO: Yes. 24 THE VIDEOGRAPHER: The time</p>	<p style="text-align: right;">Page 305</p> <p>1 are relying upon your publications, 2 correct? 3 A. Rely on. I would say they 4 may reference my paper -- 5 Q. Okay. 6 A. -- as part of their purpose 7 for that specific study. But I cannot 8 know how they cite it. Because there's 9 33,000. I cannot track on that. 10 Q. Okay. Okay that's a big 11 number, isn't it? 12 MS. MILLER: Objection. 13 THE WITNESS: Some number. 14 BY DR. RESTAINO: 15 Q. Okay. I believe we now 16 marked as Shih Exhibit 15, a paper by 17 Douglas Hanahan and Robert A. Weinberg 18 titled "The hallmarks of cancer" 19 published in Cell in January of 2000. 20 (Document marked for 21 identification as Exhibit 22 Shih-15.) 23 BY DR. RESTAINO: 24 Q. Doctor, are you familiar</p>

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<p>1 with this paper?</p> <p>2 A. I want to make sure. Cell,</p> <p>3 January 7th, 2000. That's 19 years ago.</p> <p>4 Q. Correct.</p> <p>5 A. "The hallmarks of cancer,"</p> <p>6 by Hanahan and Robert A. Weinberg. I</p> <p>7 remember, saw this paper before.</p> <p>8 Q. Okay. In fact I will</p> <p>9 represent to you that last night when I</p> <p>10 checked on this paper, this one paper has</p> <p>11 been cited 30,119 times all by itself.</p> <p>12 Have you cited this paper in</p> <p>13 your publications?</p> <p>14 A. I cannot remember. I'm on</p> <p>15 my 300 something papers --</p> <p>16 Q. Okay.</p> <p>17 A. -- whether I cite this or</p> <p>18 not.</p> <p>19 Q. Okay. If you would turn to</p> <p>20 Page 2, they have a diagram.</p> <p>21 A. You mean Figure 1, acquired</p> <p>22 capabilities of cancer?</p> <p>23 Q. Yes, sir. And they describe</p> <p>24 these as the six hallmarks of cancer, do</p>	<p>1 A. Replicative.</p> <p>2 Q. -- potential, correct?</p> <p>3 A. That's in the figure.</p> <p>4 Q. That's all in the figure in</p> <p>5 the paper that's been cited 32,000 times.</p> <p>6 Now, do you know if these</p> <p>7 authors have published a follow-up to</p> <p>8 that 2000 paper?</p> <p>9 A. I did not follow this paper.</p> <p>10 Q. Okay.</p> <p>11 (Document marked for</p> <p>12 identification as Exhibit</p> <p>13 Shih-16.)</p> <p>14 BY DR. RESTAINO:</p> <p>15 Q. We have marked as Shih-16,</p> <p>16 Hanahan and Weinberg, 2011, "Hallmarks of</p> <p>17 cancer: The next generation."</p> <p>18 Do you recall seeing this?</p> <p>19 A. I cannot recall.</p> <p>20 Q. Okay. This is published in</p> <p>21 the journal Cell. You've published in</p> <p>22 the journal Cell yourself, have you not?</p> <p>23 A. I am co-author in Cell.</p> <p>24 Q. Okay. And I will represent</p>
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<p>1 they not?</p> <p>2 A. That's the legend in the</p> <p>3 figure.</p> <p>4 Q. Okay. And one of them is</p> <p>5 self-sufficiency in growth signals.</p> <p>6 Agreed?</p> <p>7 A. You mean the green, the top</p> <p>8 one, yes.</p> <p>9 Q. Yes. And then evading</p> <p>10 apoptosis is one of the hallmarks of</p> <p>11 cancer, correct?</p> <p>12 A. Yes.</p> <p>13 Q. And then -- and alongside of</p> <p>14 that is insensitivity to antigrowth</p> <p>15 signals, correct?</p> <p>16 A. Correct.</p> <p>17 Q. And then down below they</p> <p>18 have three, the one on the left is</p> <p>19 sustained angiogenesis. Agreed?</p> <p>20 A. Yes.</p> <p>21 Q. And then tissue invasion in</p> <p>22 metastases, correct?</p> <p>23 A. I saw that.</p> <p>24 Q. And then limitless --</p>	<p>1 to you that as of yesterday, this paper</p> <p>2 by itself has been cited 34,292 times.</p> <p>3 So with the first paper, these two papers</p> <p>4 have been cited over 60,000 times.</p> <p>5 Now, we don't know, do we,</p> <p>6 of those articles that have referenced</p> <p>7 this how many times those references have</p> <p>8 been referenced, would you agree?</p> <p>9 A. How many references have</p> <p>10 been referenced, what does that mean?</p> <p>11 Q. Well, if these two papers --</p> <p>12 A. Yeah.</p> <p>13 Q. -- have been cited over</p> <p>14 60,000 times, then those 60,000 papers</p> <p>15 may have also been referenced, correct?</p> <p>16 MS. MILLER: Objection.</p> <p>17 That is not logical.</p> <p>18 THE WITNESS: They are not</p> <p>19 related to these two papers. They</p> <p>20 are just --</p> <p>21 BY DR. RESTAINO:</p> <p>22 Q. Fair enough. I'll --</p> <p>23 I'll --</p> <p>24 A. How can this be --</p>

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<p>1 MS. MILLER: When you say 2 they were cited 60,000 times, do 3 you mean 60,000 times in 60,000 4 separate papers or were they 5 sometimes cited in the same paper? 6 I just don't -- I think there's 7 some illogic in the math there 8 but -- 9 DR. RESTAINO: How can they 10 be cited in the same paper? 11 MS. MILLER: Okay. You 12 could cite both of these. 13 DR. RESTAINO: No -- okay -- 14 or both papers -- 15 MS. MILLER: If this was 16 cited 30,000 times and this was 17 cited 30,000 times. In diagrams, 18 some of them may have been cited 19 in the same paper. 20 DR. RESTAINO: Well, as it 21 happens in PubMed, when papers are 22 cited, they're cited individually. 23 The first one was cited over 24 30,000 times. The second one has</p>	<p>1 hallmarks, have they not? 2 A. I saw those boxes. 3 Q. And then down below they 4 have enabling characteristics on the 5 left, "Genome instability and mutation," 6 and on the right, "Tumor promoting 7 inflammation," correct? 8 A. Okay. Okay. I need to 9 understand this diagram, okay. So this 10 emerging hallmarks and enabling 11 characteristics. I cannot understand the 12 individual symbols, can you? This, this, 13 this, this. 14 Q. Without getting into what 15 the two individual signals are, just 16 directing your attention to the new ones 17 that they've added. And if you look over 18 on Figure 3 on the legend on the 19 right-hand side, do you see the 20 verbiage -- 21 A. I need to read. I'm sorry. 22 Q. If you look at the bottom of 23 the legend. 24 A. So additional hallmarks of</p>
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<p>1 been cited over 30,000 times. 2 Collectively, these two papers -- 3 MS. MILLER: You said then 4 those 60,000 papers. I don't 5 think you established they've been 6 cited in 60,000 papers. 7 THE WITNESS: It should be 8 60,000 citations. Not papers. 9 BY DR. RESTAINO: 10 Q. Okay. Now, let's move on 11 to, on this paper here, to Page 658. 12 Okay. And they have -- 13 A. Hold on. 14 Q. 658 and Figure 3. 15 A. So you are referring Figure 16 3? 17 Q. Yes, sir. 18 A. Imaging hallmarks and 19 enabling characteristics. 20 Q. All right. Now, in addition 21 to the six hallmarks of cancer that they 22 published in 2000, they've now added 23 deregulating cellular energetics and 24 avoiding immune destruction as emerging</p>	<p>1 cancer are involved in the pathogenesis 2 of some and perhaps... 3 (Reading to himself.) 4 Because neither capability 5 is yet generalized and fully validated. 6 Neither. 7 Thank you for your patience. 8 Q. Doctor, the final sentence 9 in that legend they write, "Inflammation 10 by innate immune cells, designed to fight 11 infections and heal wounds, can instead 12 result in their inadvertent support of 13 multiple hallmark capabilities, thereby 14 manifesting the now widely accepted" -- 15 "widely appreciated tumor-promoting 16 consequences of inflammatory responses." 17 Did I read that correctly? 18 A. This is talking about cancer 19 in general. 20 Q. Doctor, did I read that 21 correctly? 22 A. You read correctly as shown 23 in the figure legend. 24 Q. Okay. Now, do you have any</p>

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<p style="text-align: right;">Page 314</p> <p>1 objective evidence to contradict Hanahan 2 and Weinberg in this paper that's been 3 cited over 32,000 times that inflammation 4 by innate immune cells designed to fight 5 infections and heal wounds can instead 6 result in their inadvertent support of 7 multiple hallmark capabilities, thereby 8 manifesting the now widely accepted 9 tumor-promoting consequences of 10 inflammatory responses? 11 Do you disagree with that 12 statement? 13 MS. MILLER: Objection. 14 THE WITNESS: It depends. 15 If we talk about specific type of 16 cancer like ovarian high grade 17 serous carcinoma, I don't see 18 evidence, cogent evidence and 19 credible science to do that. 20 I think Dr. Weinberg is 21 saying in general, okay, take 22 every cancer, testicular cancer, 23 prostate cancer, brain tumor, 24 everything together into</p>	<p style="text-align: right;">Page 316</p> <p>1 cancer as these two gentlemen did in 2 these two separate publications that have 3 been cited over 60,000 times, that you 4 have to look at each and every cancer 5 specifically? Is that your expert 6 opinion? 7 A. So we are, as a scientist, I 8 will tell you what we're going to do. We 9 want to demonstrate the credible science 10 and the cogent evidence of biological 11 plausibility, may include those hallmarks 12 they say, but we did not find any 13 plausible evidence at this moment. 14 I think this is very good 15 guideline for the general cancer 16 biologist. But for individual one, we 17 need to demonstrate at least some of 18 these features. 19 So I did not say that I 20 disagree with Dr. Weinberg as a whole in 21 cancer biology in general, like teaching 22 medical students. 23 What I'm saying, this -- we 24 are still fighting. We try to struggle</p>
<p style="text-align: right;">Page 315</p> <p>1 consideration. 2 But it did not specify 3 ovarian cancer can do that. If 4 you have evidence that 5 Dr. Weinberg say ovarian cancer, 6 could you please show me? 7 BY DR. RESTAINO: 8 Q. Okay. So is it your opinion 9 that in discussing the hallmarks of 10 cancer, each and every cancer has to be 11 looked at individually? 12 A. That's -- 13 MS. MILLER: Objection. 14 THE WITNESS: That's a 15 totally different question. Okay. 16 You ask me another set of 17 question. 18 BY DR. RESTAINO: 19 Q. I did. It was another 20 question. 21 A. Okay. So could you repeat 22 your new question one more time. 23 Q. Yes. Is it your opinion 24 that when discussing the hallmarks of</p>	<p style="text-align: right;">Page 317</p> <p>1 very much in our laboratory to find those 2 evidence. So that's our aim. We want to 3 find this evidence. But we don't have 4 any evidence to show in ovarian cancer 5 research. 6 Also, I want to tell you, 7 Nobel Prize Laureate, the finding -- has 8 been cited so many times. 9 So, again, I'm looking at 10 the science, not where it come from, the 11 institution, authors, and citations. 12 Citation's a good indicator, but it does 13 not mean too much. Especially as a 14 review paper. 15 Q. You yourself have reported 16 that you've been referenced over 30,000 17 times twice today, correct, Doctor? 18 A. Yes, I just tell you. 19 That's a number that I tell you. But I 20 cannot tell you that my reputation is 21 solely based on my citation. It's based 22 on my research findings. 23 Q. You state, "We try to 24 struggle very much in our laboratory to</p>

<p style="text-align: right;">Page 318</p> <p>1 find those evidence, so that's our aim. 2 We want to find this evidence. We don't 3 have any evidence to show in ovarian 4 cancer research." 5 Do you have any evidence to 6 show that the hallmarks and emerging 7 characteristics as listed by Hanahan and 8 Weinberg do not apply to ovarian cancer? 9 MS. MILLER: Objection. 10 THE WITNESS: I need to 11 review your question. Okay? 12 What I said, there's no 13 evidence to support that ovarian 14 high grade serous carcinoma if 15 this is the type we are talking 16 about, because otherwise it's so 17 confusing, because every type is 18 different. That's the problem 19 with epidemiologic studies. 20 So we'll go back. 21 So what you said is do not 22 apply to ovarian cancer. What 23 does that mean? 24 I said we don't have</p>	<p style="text-align: right;">Page 320</p> <p>1 carcinoma, renal cell carcinoma, 2 endometrioid carcinoma. 3 I don't find any cogent 4 evidence for this biological 5 mechanism in the literature. 6 DR. RESTAINO: I'm going to 7 move to strike as nonresponsive. 8 BY DR. RESTAINO: 9 Q. Doctor, in the form of 10 ovarian cancer that you study, any form, 11 you can pick the form, whatever form you 12 study, one hallmark of ovarian cancer is 13 that it sustains proliferative signaling 14 and keeps going, correct? That's a 15 hallmark of every cancer known to man, 16 correct? 17 MS. MILLER: Objection. 18 THE WITNESS: Can you say 19 that one more time? Every single 20 tumor cells? 21 BY DR. RESTAINO: 22 Q. Every single tumor -- 23 A. Tumor. Not tumor cells, 24 okay.</p>
<p style="text-align: right;">Page 319</p> <p>1 evidence to show, including, okay, 2 this hallmarks in ovarian cancer 3 precursor lesions, the high grade 4 precursor means STIC and p53 5 signature. We don't have any 6 evidence to show. It doesn't mean 7 no evidence. It doesn't mean it's 8 not applicable. Okay. We just 9 don't have evidence to show. 10 There's no credible science. 11 BY DR. RESTAINO: 12 Q. You don't have evidence to 13 contradict these two researchers, 14 correct? 15 MS. MILLER: Objection. 16 THE WITNESS: These two 17 researchers, they claim -- they 18 come up with these features in 19 cancer biology in general. It 20 cannot be applicable to specific 21 cancer type, like, for example, 22 cholangiocarcinoma, sarcoma, high 23 grade serous carcinoma, low grade 24 serous carcinoma, clear cell</p>	<p style="text-align: right;">Page 321</p> <p>1 Q. -- undergoes sustained 2 proliferative signaling. That's what 3 makes it an out-of-control cancer, 4 correct? Every cancer. 5 MS. MILLER: Objection. 6 THE WITNESS: Not in their 7 precursor lesion. That would be 8 another different landscape. You 9 talk about cancer including 10 precursor in situ cancer, or are 11 you -- you mean the metastases? 12 If you say metastases, of course, 13 they can expand, uncontrolled 14 proliferation. 15 BY DR. RESTAINO: 16 Q. I'm talking about -- 17 A. When you talk about cancer 18 precursor, that's a different thing. 19 And this is our focus today, 20 is whether talc and -- or asbestos can 21 cause ovarian cancer. We should focus on 22 the precursor lesion, not the big 23 blown -- the full-blown, the cancer that 24 kill patients.</p>

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<p>1 Q. Okay. I know that's what 2 you want to focus on, but there are many 3 other experts that are not focused on 4 that and they're looking at the totality 5 of the evidence of linking ovarian cancer 6 with inflammation and inflammation 7 secondary to talc. 8 And inflammation-promoting 9 properties has been listed by these 10 authors as widely appreciated in the 11 medical field, correct? 12 A. Could you show me the -- the 13 references -- references to show this 14 part? 15 Q. I've showed you the article. 16 A. That's a review. 17 Q. Okay. 18 A. But do you have any single 19 paper that you claim that you were happen 20 in ovarian cancer? 21 Q. Do you have a single paper 22 that shows that inflammation is not 23 pro-growth in the cancer arena? 24 MS. MILLER: Objection.</p>	<p>1 MR. LOCKE: Objection. 2 THE WITNESS: I think I 3 answered your question in this 4 morning's discussion, I believe. 5 What I said is scientists -- okay. 6 I will say science is evidence -- 7 evidence-driven, evidence-driven. 8 We can prove positivity to 9 show the evidence, but we cannot 10 prove negativity, because this 11 against the science practice. 12 This is not logic in science. How 13 can we prove there is no -- no 14 tumor in a person? We need to see 15 the tumor, so we can say, oh, you 16 are a cancer patient, until we 17 find it. 18 DR. RESTAINO: I'm going to 19 move to strike. 20 BY DR. RESTAINO: 21 Q. Doctor, what paper, 22 peer-reviewed, published, are you relying 23 upon for the basis of your opinion that 24 inflammation plays no role in the growth</p>
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<p>1 BY DR. RESTAINO: 2 Q. A single paper that shows 3 that -- that inflammation, whether it's 4 caused by the cancer itself or the body's 5 innate response to that cancer, a single 6 paper that shows that inflammation does 7 not promote the growth of the cancer? 8 MS. MILLER: Objection. 9 Please let me get my objection. I 10 know you're excited to answer. 11 But that was objectionable. 12 THE WITNESS: Yeah, right. 13 BY DR. RESTAINO: 14 Q. Okay. What don't I 15 strike -- do you need the question asked 16 again, Doctor? 17 A. Please. 18 Q. Okay. Doctor, can you show 19 us or refer us to a single paper that is 20 of cogent evidence which shows that 21 inflammation, whether caused by the tumor 22 or promoting the tumor does not affect 23 the growth of cancer? 24 MS. MILLER: Objection.</p>	<p>1 promotion of ovarian cancer? 2 MS. MILLER: Objection. 3 He's answered this question 4 multiple times, and it was an 5 objectionable question even before 6 he answered it multiple times. 7 MS. PARFITT: "Objection" is 8 fine. 9 THE WITNESS: I answer your 10 questions multiple times, and my 11 answer was remains the same if you 12 keep asking me 100 times. 13 BY DR. RESTAINO: 14 Q. I'm sorry. I -- I missed 15 your -- the name of the paper that you -- 16 that you are relying upon. I'm -- I'm 17 sharing with you a paper that has been 18 cited over 32,000 times which states that 19 it is now widely appreciated 20 tumor-promoting consequences of 21 inflammatory response. 22 Your response was that it 23 doesn't apply to ovarian cancer. I'm 24 asking for one paper --</p>

<p style="text-align: right;">Page 326</p> <p>1 MR. LOCKE: Objection. 2 BY DR. RESTAINO: 3 Q. -- that is cogent evidence 4 that the tumor-promoting consequences of 5 inflammatory response does not apply to 6 ovarian cancer. 7 MS. MILLER: Objection. 8 Same -- I'll -- 9 THE WITNESS: Same answer. 10 I can repeat one more time. 11 BY DR. RESTAINO: 12 Q. Give me the name of the 13 paper. 14 A. I can give you one more time 15 my answer. 16 Q. I want the name of the 17 paper. 18 A. Science -- science, 19 practicing science, as a scientist, our 20 job is to find the positive evidence to 21 support hypothesis. This by no means we 22 can come up with negative results because 23 this is not logic in science. 24 Q. You can't come out with</p>	<p style="text-align: right;">Page 328</p> <p>1 MS. SHARKO: Object to the 2 form. 3 THE WITNESS: No, what I 4 said is that's the scientist's 5 job. Okay. If you have a 6 hypothesis, talcum powder can 7 cause ovarian cancer, you need to 8 show the cogent evidence and 9 credible science to support the 10 biological plausibility. That's 11 what I said. It doesn't mean I -- 12 okay, I need to review those 13 evidence -- 14 BY DR. RESTAINO: 15 Q. Okay. And -- 16 A. -- to see whether they are 17 credible or not. 18 Q. And have you reviewed 19 evidence that shows that inflammation 20 does not promote ovarian cancer? 21 MS. MILLER: Objection. 22 Asked and answered like 15 times. 23 THE WITNESS: I already 24 answered.</p>
<p style="text-align: right;">Page 327</p> <p>1 negative results -- 2 A. Because this a logic 3 problem. Okay. We cannot prove 4 negativity. The science is -- is 5 evidence driven. 6 Q. Okay. 7 A. Only evidence there can 8 become positive. Okay. With a positive, 9 you can claim something to be further 10 tested. But no one in the whole wide 11 world can prove negativity. Period. 12 Q. Okay. So you can't give me 13 the name of a single paper? 14 A. The answer is I just -- 15 MS. MILLER: Objection. 16 Doctor, please let me object. 17 BY DR. RESTAINO: 18 Q. Okay. And -- and, Doctor, 19 it is your expert opinion that it is your 20 job to come up with positive evidence to 21 support a hypothesis, and by no means you 22 can come up with negative results, 23 because that's not logic in science, 24 correct?</p>	<p style="text-align: right;">Page 329</p> <p>1 BY DR. RESTAINO: 2 Q. And you gave me the name of 3 the -- okay, then, what is the -- what is 4 the lead author's name of the paper that 5 you were relying upon? 6 MS. MILLER: Objection. 7 That's argumentative. That's 8 misstating the witness's 9 testimony. And he's answered this 10 question in a hundred different 11 forms multiple, multiple times. 12 BY DR. RESTAINO: 13 Q. Doctor, you can't name a 14 single paper, can you? 15 MS. MILLER: Objection. 16 THE WITNESS: What kind of 17 paper you are referring to? 18 BY DR. RESTAINO: 19 Q. A peer-reviewed published 20 paper that contradicts Hanahan and 21 Weinberg's paper, which has been cited 22 32,000 times, which talks about the 23 widely appreciated tumor-promoting 24 properties of inflammation.</p>

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<p>1 MS. MILLER: Objection. 2 BY DR. RESTAINO: 3 Q. Doctor, are you thinking, 4 or -- 5 MS. SHARKO: Well, you all 6 were talking. 7 MS. MILLER: I don't even 8 know where we are. I think -- 9 MS. SHARKO: Same question. 10 MS. MILLER: Okay. Same 11 question, same objection. It's 12 been asked and answered in many, 13 many different ways. 14 MS. PARFITT: The doctor 15 needs to answer the question. 16 MS. MILLER: The doctor has 17 answered the question. 18 MS. PARFITT: The doctor has 19 not answered the question. The 20 doctor -- 21 THE WITNESS: I believe I 22 answered the question. 23 BY DR. RESTAINO: 24 Q. You've given -- you've given</p>	<p>1 the tumor-promoting properties of 2 inflammation is widely appreciated? 3 MS. MILLER: Objection. 4 THE WITNESS: In my research 5 team, we have many top priority 6 projects. And this is not the 7 research area we want to be 8 engaged. We want to develop early 9 detection methods and effective 10 treatments for ovarian cancer 11 patients. 12 BY DR. RESTAINO: 13 Q. Is that no? 14 MS. MILLER: Objection. 15 THE WITNESS: What has been 16 no? 17 BY DR. RESTAINO: 18 Q. Is your answer no, that 19 you've not published a paper that refutes 20 Hanahan and Weinberg's statement that the 21 tumor-promoting properties of 22 inflammation are widely appreciated? 23 MS. MILLER: Objection. 24 THE WITNESS: I answered</p>
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<p>1 me the name of the article you're relying 2 upon? 3 A. I said -- I answered -- 4 MS. MILLER: That is a 5 misleading question. 6 MS. PARFITT: Objection to 7 form, Counsel, is really the -- 8 the appropriate response. We 9 tried to be patient with that. 10 MS. MILLER: Well, I'm 11 trying to be patient -- 12 MS. SHARKO: Well, you guys 13 also can't just make editorial 14 comments on his answer. 15 MS. PARFITT: I don't think 16 that we have. 17 DR. RESTAINO: The record 18 will report what the record 19 reports. 20 MS. MILLER: You have the 21 answer multiple times. 22 BY DR. RESTAINO: 23 Q. Have you ever published a 24 paper that contradicts the statement that</p>	<p>1 your question before. 2 THE VIDEOGRAPHER: Counsel, 3 we need to go off the record. The 4 time is 3:50 p.m. We are going 5 off the record. 6 (Short break.) 7 THE VIDEOGRAPHER: The time 8 is 3:56 p.m. We are back on the 9 record. 10 DR. RESTAINO: I'm going to 11 ask Madam Court Reporter, 12 Michelle, to mark the deposition 13 regarding the discussion we had 14 regarding an article refuting the 15 Hanahan and Weinberg analysis. 16 BY DR. RESTAINO: 17 Q. And, Doctor, I want to 18 change channels, so to speak. And let's 19 go to your expert report. And if you 20 would look on Page 5, and there you have 21 a criticism of the cancer cell lines that 22 Dr. Saed has used, correct? 23 A. That's my opinion. 24 Q. Okay. Down at the bottom of</p>

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<p style="text-align: right;">Page 334</p> <p>1 it -- one, two, three, four -- five lines 2 up you state, "Another problem with the 3 study design is the researchers 4 mistakenly used an A2780 cell line as an 5 ovarian high grade serous cancer cell 6 line. But in fact A2780 is unlikely an 7 ovarian high-grade serous cancer line and 8 should not have been relevant in this 9 study, reflecting the limited knowledge 10 of the research group in studying ovarian 11 cancer (Anglesio, et al., 2013; 12 Domcke" -- D-O-M-C-K-E -- "et al., 13 2013.)" 14 Did I read that correctly, 15 Doctor? 16 A. That is what is my opinion. 17 Q. Now, was your opinion there 18 derived from reviewing the Saed paper 19 itself? 20 A. You mean this publication's 21 precursor? 22 Q. That publication? It's -- 23 A. No, its precursor, meaning 24 the manuscript.</p>	<p style="text-align: right;">Page 336</p> <p>1 MS. MILLER: If you look at 2 Dr. Shih's expert report, I think 3 what you said misstates what is 4 here. He has two sections in his 5 expert report as I'm reading it 6 now. 7 One says Dr. Saed's 8 statement in his expert report. 9 Another says Dr. Saed's in-press 10 paper in Reproductive Science. So 11 are you focused on the expert 12 report or Reproductive Science 13 manuscript now? 14 DR. RESTAINO: I'm focused 15 on Dr. Shih's expert report on 16 Page 5. 17 MS. MILLER: Right. 18 DR. RESTAINO: Where he has 19 a paragraph there titled "Use of 20 cancer cell lines." 21 MS. MILLER: Right. And 22 that refers to Dr. Saed's expert 23 report, not Dr. Saed's manuscript. 24 So you misstated that. I just</p>
<p style="text-align: right;">Page 335</p> <p>1 Q. Okay. And you looked at 2 that, correct? 3 And let's look at the 4 study -- 5 MS. MILLER: Wait a minute. 6 This is under a part of his report 7 that says Dr. Saed's statements in 8 his expert report, not the part of 9 the report that says Dr. Saed's 10 in-press paper. There are two 11 sections of this report. One 12 refers -- I just want to make sure 13 that the record is clear because I 14 think that was not accurate. 15 Dr. Saed's statement in his 16 expert report, that's where he 17 discusses that. 18 Then on Page 6 it says 19 Dr. Saed's in-press paper. So 20 this is based on the expert 21 report, based on looking at the 22 report. That's what it says. 23 DR. RESTAINO: What is based 24 on the expert report?</p>	<p style="text-align: right;">Page 337</p> <p>1 wanted to get that clear on the 2 record. 3 DR. RESTAINO: Okay. Duly 4 noted. 5 BY DR. RESTAINO: 6 Q. Okay. I would like to take 7 a look at Dr. Saed's published paper? 8 A. This one. In Reproductive 9 Science, 2019? 10 Q. Correct. If you would turn, 11 Doctor, to the second page on the lower 12 left-hand side there's a section titled 13 "Material and Methods." And then "Cell 14 Lines." 15 Do you see that, sir? 16 A. Right. I saw it here. 17 Q. Okay. And there they 18 discuss, under their cells and the cell 19 lines, that they use ovarian cancer cells 20 capital S -- all caps -- SK-OV-3(ATCC), 21 A2780 (Sigma-Aldrich at St. Louis, 22 Missouri), and TOV112D (a kind gift from 23 Gen Sheng" -- S-H-E-N-G -- "Wu" -- W-U -- 24 "at Wayne State University, Detroit,</p>

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<p>1 Michigan), and normal cells, human 2 macrophages (EL-1; ATC, Manassas, 3 Virginia), human primary normal ovarian 4 epithelial cells (Cell Biologic Chicago, 5 Illinois), human ovarian epithelial cells 6 (HOSEpiC; ScienCel" -- S-C-I-E-N-C-E-L -- 7 "Research Laboratories Incorporated, 8 Carlsbad, California), and immortalized 9 human fallopian tubes secretory 10 epithelial cells (FT33; Applied 11 Biological Materials, Richmond, British 12 Columbia, Canada) were used." 13 Did I read that correctly, 14 Doctor, with all those letters and 15 everything? 16 A. This were -- this sentence 17 has been written in this paper. 18 Q. Okay. They use normal cell 19 macrophages in their study, did they not? 20 MS. MILLER: Objection. 21 BY DR. RESTAINO: 22 Q. That's the fourth line? 23 A. I don't think they're normal 24 anymore. If it become a cell line,</p>	<p>1 normal epithelial -- Cell Biologicals, 2 Chicago, Illinois. 3 I never know this so-called 4 normal ovarian epithelial cells, because 5 every time, when they culture the 6 epithelial cells, they have really finite 7 life spans. They cannot -- they are not 8 cancer, right? So as we remember vividly 9 from the Weinberg's charts, this normal 10 cells cannot proliferate all the time. 11 But in order for that 12 society to study in culture, they need to 13 expand that. And when they expand, they 14 are not normal epithelial cell already. 15 When we look at normal epithelial cells 16 in human tissue, they may not be 17 proliferative. So I don't think how 18 relevant this cell line will be to this 19 study. 20 Q. Have you ever used the human 21 primary normal ovarian epithelial cells 22 from Cell Biologics, Chicago, Illinois? 23 A. I cannot recall. But if I 24 did, we are doing -- we are asking</p>
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<p>1 meaning they're immortalized, and the 2 macrophages, as you know, according to 3 Dr. Weinberg, the charts, they are 4 normal, but the cell line, they can be 5 maintained in tissue culture, and they 6 can divide all the time. 7 So this is -- by no means is 8 normal macrophages. It has some -- as 9 Dr. Weinberg said, just as you, candidly, 10 as you do to me, that's one of the 11 feature of cancer. 12 Q. But in normal cells, like in 13 normal macrophages, they have a limited 14 number of mitotic events before they 15 begin to die out, correct? 16 A. I don't even know whether 17 human macrophages can ever replicate in 18 tissue culture, because they are 19 terminally differentiated immune cells. 20 Q. Okay. Well, in addition to 21 using the macrophages as listed in the 22 paper, they also used human primary 23 normal ovarian epithelial cells, correct? 24 A. You mean the human primary</p>	<p>1 different scientific questions, okay. 2 It's totally irrelevant. 3 Q. Okay. In addition for his 4 study, they used human ovarian epithelial 5 cells or HOSEpiC obtained from ScienCel 6 Research Laboratories, correct? 7 A. Yeah, they're in California. 8 This has been written. 9 Q. Okay. And as I'm going 10 through this, the only cell line that 11 you're criticizing in your expert report 12 is that they use the A2780, correct? 13 A. Let me go back to my report. 14 Q. Yes, sir. It's Page 5, 15 paragraph titled "Use of Cancer Cell 16 Lines." 17 MS. MILLER: Are you asking 18 anywhere in his report if that's 19 the only place -- 20 THE WITNESS: I saw this 21 paragraph. 22 At the time I believe this 23 is the most important deficiency 24 in the methodology, meaning cell</p>

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<p>1 lines cannot -- ovarian cancer</p> <p>2 cell lines cannot be used to</p> <p>3 answer the question of where it</p> <p>4 starts. You need to start from</p> <p>5 the normal epithelial cells. So</p> <p>6 this is -- I -- this is totally</p> <p>7 methodology incorrect.</p> <p>8 BY DR. RESTAINO:</p> <p>9 Q. Okay. And Dr. -- the Saed</p> <p>10 team also utilized immortalized human</p> <p>11 fallopian secretory epithelial cells,</p> <p>12 FT33, obtained from Applied Biological</p> <p>13 Materials, correct?</p> <p>14 A. It has been written. But</p> <p>15 that's a really bad idea.</p> <p>16 Q. Okay. Whether it's your</p> <p>17 opinion of a good idea or a bad idea,</p> <p>18 did -- do you discuss in your expert</p> <p>19 report the fact that they use these --</p> <p>20 these various cell lines?</p> <p>21 A. To the scientific community,</p> <p>22 I think this is so obvious flaw. So I</p> <p>23 just mention the ovarian cancer cell line</p> <p>24 issue here. But I think everybody will</p>	<p>1 hyphen in it.</p> <p>2 MS. MILLER: Oh, it's got no</p> <p>3 hyphen.</p> <p>4 THE WITNESS: It's the same,</p> <p>5 everybody know SK-OV-3.</p> <p>6 MS. MILLER: I'm sorry.</p> <p>7 That was -- object to foundation.</p> <p>8 I retract what I said. I just was</p> <p>9 looking right at the word.</p> <p>10 BY DR. RESTAINO:</p> <p>11 Q. Okay. Doctor.</p> <p>12 A. Yes.</p> <p>13 Q. Now, talking about the A2780</p> <p>14 cell line. In fact, despite your</p> <p>15 criticism, the medical literature is</p> <p>16 replete with research articles pertaining</p> <p>17 to ovarian cancer which utilize A2780,</p> <p>18 correct?</p> <p>19 A. Could you repeat the</p> <p>20 question one more time, slowly.</p> <p>21 Q. Yes. The medical literature</p> <p>22 is filled with current research articles</p> <p>23 pertaining to ovarian cancer and</p> <p>24 utilizing the A2780 cell line?</p>
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<p>1 agree, this is totally not correct</p> <p>2 methodology to answer the specific</p> <p>3 question about the carcinogenesis.</p> <p>4 Q. The Saed team tested three</p> <p>5 cancer cell lines in addition to normal</p> <p>6 cell lines and immortalized cell lines,</p> <p>7 did they not?</p> <p>8 A. I will not say normal cell</p> <p>9 line. A cell line cannot be normal</p> <p>10 anymore.</p> <p>11 Q. They used ovarian cancer</p> <p>12 cells, SK-OV-3, correct?</p> <p>13 A. Yes.</p> <p>14 Q. That's not listed in your</p> <p>15 expert report, is it?</p> <p>16 MS. MILLER: That's a lie.</p> <p>17 It's right here on Page 6. I'm</p> <p>18 looking at it.</p> <p>19 DR. RESTAINO: Well, it's</p> <p>20 not a lie. I just -- I just</p> <p>21 word-searched it.</p> <p>22 MS. MILLER: Just -- okay.</p> <p>23 SK-OV-3? I'm looking at it.</p> <p>24 DR. RESTAINO: It's got no</p>	<p>1 MR. LOCKE: Objection.</p> <p>2 THE WITNESS: This cell line</p> <p>3 has been used in the past without</p> <p>4 knowing that the origin is now</p> <p>5 ovarian cancer.</p> <p>6 And as a result, as you can</p> <p>7 see, the -- the reference I cited,</p> <p>8 Domcke 2013 and Anglesio 2013. I</p> <p>9 think that's why this is so</p> <p>10 important. I think these are two</p> <p>11 papers can allow, as a scientist,</p> <p>12 we try very hard to do ovarian</p> <p>13 cancer research, that we need to</p> <p>14 be really careful about our cell</p> <p>15 lines and the most up-to-date</p> <p>16 knowledge we should perform in</p> <p>17 tissue culture studies.</p> <p>18 BY DR. RESTAINO:</p> <p>19 Q. Doctor, would you be</p> <p>20 surprised if I represent to you that</p> <p>21 since January 1st of 2018, so we're</p> <p>22 dealing with maybe 15 months, not going</p> <p>23 back to Domcke in 2013. Since</p> <p>24 January 1st, 2018, 139 peer-reviewed</p>

<p style="text-align: right;">Page 346</p> <p>1 articles have been published utilizing</p> <p>2 the A2780 ovarian cancer cell line?</p> <p>3 MR. LOCKE: Objection.</p> <p>4 BY DR. RESTAINO:</p> <p>5 Q. Would that surprise you,</p> <p>6 sir?</p> <p>7 MS. MILLER: Objection.</p> <p>8 THE WITNESS: That's</p> <p>9 unfortunate that scientists did</p> <p>10 not be aware of that. Some</p> <p>11 scientists may be aware of that,</p> <p>12 but they still use A2780.</p> <p>13 You know why? Because this</p> <p>14 cell line is very easy to grow and</p> <p>15 people love it, because it's -- it</p> <p>16 proliferates very well. So people</p> <p>17 know maybe, they know that this is</p> <p>18 not a good model. But they still</p> <p>19 continue using it, pretending</p> <p>20 nobody know this trick.</p> <p>21 BY DR. RESTAINO:</p> <p>22 Q. So it is your subjective</p> <p>23 opinion that the A2780 is not an adequate</p> <p>24 cell line to use, but objectively</p>	<p style="text-align: right;">Page 348</p> <p>1 are aware of that publication as of last</p> <p>2 week?</p> <p>3 MS. MILLER: Objection.</p> <p>4 THE WITNESS: In order -- in</p> <p>5 order to answer your question, I</p> <p>6 need to see that.</p> <p>7 BY DR. RESTAINO:</p> <p>8 Q. Is carboplatin the most</p> <p>9 used, widely used chemotherapy regimen</p> <p>10 for ovarian cancer?</p> <p>11 A. I don't really --</p> <p>12 MS. MILLER: Objection.</p> <p>13 THE WITNESS: This is</p> <p>14 totally irrelevant. We are</p> <p>15 talking about the carcinogenesis.</p> <p>16 Ovarian cancer precursor,</p> <p>17 talcum powder, including Johnson &</p> <p>18 Johnson product, can cause ovarian</p> <p>19 cancer, then we are talking about</p> <p>20 the technical part of cell lines.</p> <p>21 I think we are off track.</p> <p>22 BY DR. RESTAINO:</p> <p>23 Q. Then would you withdraw your</p> <p>24 criticism of Dr. Saed's use of A2780?</p>
<p style="text-align: right;">Page 347</p> <p>1 researchers continue to publish the</p> <p>2 results including for treatment of</p> <p>3 ovarian cancer; isn't that correct?</p> <p>4 MS. MILLER: Objection.</p> <p>5 MR. LOCKE: Objection.</p> <p>6 BY DR. RESTAINO:</p> <p>7 Q. I'll represent to you,</p> <p>8 Doctor, functional and transcriptomic</p> <p>9 characterization of carboplatin resistant</p> <p>10 A2780 ovarian cancer cell line was</p> <p>11 published in biological research last</p> <p>12 week. And these researchers are looking</p> <p>13 at this A2780 ovarian cancer cell line</p> <p>14 that they've now made carboplatin</p> <p>15 resistant in order to determine what they</p> <p>16 can do to help patients who become</p> <p>17 resistant to carboplatin therapy. Are</p> <p>18 you aware of that, Doctor?</p> <p>19 MS. MILLER: Objection.</p> <p>20 THE WITNESS: I need to see</p> <p>21 the reference. Do you have the</p> <p>22 paper with you?</p> <p>23 BY DR. RESTAINO:</p> <p>24 Q. I'm just asking you if you</p>	<p style="text-align: right;">Page 349</p> <p>1 MS. MILLER: Objection.</p> <p>2 THE WITNESS: No. It's</p> <p>3 wrong --</p> <p>4 BY DR. RESTAINO:</p> <p>5 Q. Then it is -- then it is</p> <p>6 irrelevant to our discussion. I know you</p> <p>7 want to talk about your work. But we're</p> <p>8 also here to talk about the flaws you</p> <p>9 feel that Dr. Saed has in his paper?</p> <p>10 A. Okay.</p> <p>11 Q. And my representation --</p> <p>12 representation to you is that despite</p> <p>13 your subjective opinion, A2780 is still</p> <p>14 being widely used and published up to</p> <p>15 last week.</p> <p>16 MS. MILLER: Objection.</p> <p>17 MS. SHARKO: That's not a</p> <p>18 question.</p> <p>19 MS. MILLER: Please give me</p> <p>20 time me object.</p> <p>21 That's true too.</p> <p>22 THE WITNESS: What do you</p> <p>23 mean widely used?</p> <p>24 BY DR. RESTAINO:</p>

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<p>1 Q. How about 139 publications.</p> <p>2 A. As compared to what?</p> <p>3 Q. As compared to zero</p> <p>4 publications?</p> <p>5 A. Where does zero come from?</p> <p>6 Q. Well, if it was no longer a</p> <p>7 recognized viable cell line, then people</p> <p>8 would stop using it and publishing it.</p> <p>9 Peer reviewers wouldn't approve it, and</p> <p>10 journals wouldn't publish it; isn't that</p> <p>11 true?</p> <p>12 MS. MILLER: Objection.</p> <p>13 MR. LOCKE: Objection.</p> <p>14 MS. MILLER: We are</p> <p>15 synchronized.</p> <p>16 THE WITNESS: That's why</p> <p>17 good science is so important;</p> <p>18 otherwise, how can we cure ovarian</p> <p>19 cancer now, right? It's because</p> <p>20 we need to really update and keep</p> <p>21 abreast of new knowledge, and</p> <p>22 using the correct methodologies.</p> <p>23 So I only care about the science,</p> <p>24 whether the credible science,</p>	<p>1 little bit confusing, because, as</p> <p>2 I noted -- and I think this is why</p> <p>3 you didn't find the SKOV thing.</p> <p>4 But this -- there's a section on</p> <p>5 Dr. Saed's statements in his</p> <p>6 expert report as one, and then</p> <p>7 Dr. Saed's in-press paper, and so</p> <p>8 CA-125 is covered both on Pages 5</p> <p>9 and 7. And that was also what</p> <p>10 happened with the cell lines, why</p> <p>11 you didn't find it.</p> <p>12 So just specify whether</p> <p>13 you're referring to the CA-125</p> <p>14 discussion on Page 5 or Page 7.</p> <p>15 DR. RESTAINO: Okay. I'm</p> <p>16 looking --</p> <p>17 MS. MILLER: That was some</p> <p>18 confusion in the last round of</p> <p>19 questions.</p> <p>20 DR. RESTAINO: I appreciate</p> <p>21 that. Thank you. Yes.</p> <p>22 BY DR. RESTAINO:</p> <p>23 Q. I'm looking at your</p> <p>24 paragraph on Page 5 wherein you -- it's</p>
Page 351	Page 353
<p>1 cogent evidence can support</p> <p>2 biological plausibility regarding</p> <p>3 this issue. That's my concern.</p> <p>4 And this is incorrect cell lines</p> <p>5 to be used. Totally incorrect and</p> <p>6 not relevant to ovarian cancer.</p> <p>7 BY DR. RESTAINO:</p> <p>8 Q. Have you conducted research</p> <p>9 of PubMed to look at how many individuals</p> <p>10 are still publishing using A2780 since</p> <p>11 January 1st of 2018?</p> <p>12 MS. MILLER: Objection.</p> <p>13 THE WITNESS: I have so many</p> <p>14 thing to do. Top priority. This</p> <p>15 is incorrect methodology to be</p> <p>16 used, why it bother me.</p> <p>17 BY DR. RESTAINO:</p> <p>18 Q. Okay. I'll move on. Let's</p> <p>19 take a look at your expert report where</p> <p>20 you talk about the irrelevance of CA-125.</p> <p>21 A. Which page? I'm sorry.</p> <p>22 Q. I believe it's on Page 5?</p> <p>23 MS. MILLER: So again, I</p> <p>24 just want to point out that it's a</p>	<p>1 titled "Irrelevance of CA-125."</p> <p>2 Do you see that, sir?</p> <p>3 A. Yes.</p> <p>4 DR. RESTAINO: Jessica, are</p> <p>5 you on the same page?</p> <p>6 MS. MILLER: Yep.</p> <p>7 BY DR. RESTAINO:</p> <p>8 Q. Okay. Now, CA-125 stands</p> <p>9 for cancer antigen 125, correct?</p> <p>10 A. Correct.</p> <p>11 Q. And an antigen is a toxin or</p> <p>12 a foreign substance for which the</p> <p>13 immune -- the body has an immune</p> <p>14 response, including the production of</p> <p>15 antibodies, correct?</p> <p>16 A. No.</p> <p>17 Q. Well, how -- okay. Then</p> <p>18 I'll use your definition. How do you</p> <p>19 define an antigen?</p> <p>20 A. It's not my definition.</p> <p>21 It's a scientific definition. It's not</p> <p>22 only me. It's everybody accept.</p> <p>23 Q. Sir, I'll use your</p> <p>24 definition or the definition that you</p>

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<p style="text-align: right;">Page 354</p> <p>1 have adopted from the scientific 2 community. What is an antigen? 3 A. Antigen is the protein that 4 can be recognized by our immune system. 5 Q. CA-125 is expressed as a 6 membrane-bound protein on the surface of 7 cells that undergo metaplastic 8 differentiation into mullerian 9 epithelium, correct? 10 MS. MILLER: Objection. Are 11 you reading from something? 12 DR. RESTAINO: My notes. 13 THE WITNESS: What do you 14 mean "under surface of cells"? I 15 can't understand. 16 BY DR. RESTAINO: 17 Q. Oh, the protein on the 18 surface of the cell. 19 A. Oh, on the cell. Not under. 20 Q. Right. Doctor, I'll adopt 21 your definition of an antigen, but that's 22 what CA-125 -- 23 A. Well, I'm not finished. 24 MS. MILLER: Are you</p>	<p style="text-align: right;">Page 356</p> <p>1 biomarker, correct? 2 A. You refer to the Line 3, is 3 definitely not a cancer-specific 4 biomarker. Is that one? 5 Q. The word "biomarker" is used 6 several times. I'm just going to ask you 7 what you mean by biomarker? 8 A. Oh. Okay. 9 MS. MILLER: Objection. 10 THE WITNESS: Biomarker -- 11 biomarker is a term generally used 12 in different research and by 13 different meanings for different 14 scientists and medical doctors. 15 By the CA-125, is biomarkers, 16 meaning it is something associated 17 with ovarian cancer but not a 18 precursor. That's the point. Not 19 a precursor, but ovarian cancer. 20 So what happened is 21 CA-125 -- usually I call it MUC16, 22 same thing -- is expressed by the 23 mullerian, normal mullerian duct 24 epithelial cells.</p>
<p style="text-align: right;">Page 355</p> <p>1 withdrawing that question? Or do 2 you want him to answer that 3 question? I just -- again -- 4 THE WITNESS: I'm not 5 finished reading your thoughts. 6 BY DR. RESTAINO: 7 Q. Okay. 8 A. CA-125 is also known as a 9 mucin 16, was first identified by Dr. Bob 10 Bast at M.D. Anderson Cancer Center. 11 So, I am not sure this is 12 correct. You said, metaplastic 13 differentiation and into mullerian 14 epithelial cells. I don't know that's 15 correct, unless you show me the 16 reference. 17 Q. Do you know it to be 18 incorrect? 19 A. I need to see the reference 20 to make sure you are correct. 21 Q. Okay. I'll -- you then in 22 your paragraph that we're reading from, 23 irrelevance of CA-125 finding, you talk 24 about cancer specific -- or cancer</p>	<p style="text-align: right;">Page 357</p> <p>1 So every woman has a low 2 level of that. But ovarian 3 cancer, when they become 4 transformed -- are you ready? 5 If they are transformed, 6 they have more and more cells. It 7 may not be that individual tumor 8 cells express higher, but because 9 the number is more. 10 So this is very different. 11 They are not causal. They are 12 just biomarkers. There are so 13 many biomarkers without known 14 etiology or biological mechanism. 15 In terms of tumor 16 progression -- I mean in terms of 17 tumor initiation. 18 So it has been shown, CA-125 19 in a serum can be a marker to 20 follow, monitor, disease 21 progression, but never be used as 22 biomarker to identify ovarian 23 cancer in the detection and 24 screening.</p>

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<p style="text-align: right;">Page 358</p> <p>1 And it is by no means is it</p> <p>2 important in the transition of</p> <p>3 normal fallopian tube to a STIC or</p> <p>4 p53 signature.</p> <p>5 So FDA approved, this can be</p> <p>6 followed, monitored to see if we</p> <p>7 have a cancer. I think this is</p> <p>8 important because that's --</p> <p>9 DR. RESTAINO: Doctor, I'm</p> <p>10 going to move to strike.</p> <p>11 BY DR. RESTAINO:</p> <p>12 Q. I just asked you what's your</p> <p>13 definition of a biomarker. If I asked</p> <p>14 you the time, I don't need for you to</p> <p>15 make a watch. I just want to know the</p> <p>16 time.</p> <p>17 What is a biomarker?</p> <p>18 A. Biomarker is different</p> <p>19 types, tissue bio marker, serum</p> <p>20 biomarkers. Do you want me to continue</p> <p>21 or not?</p> <p>22 Q. I just want you to define a</p> <p>23 biomarker so we get to the --</p> <p>24 A. That's why I'm going to</p>	<p style="text-align: right;">Page 360</p> <p>1 mean indicative?</p> <p>2 Q. Suggesting.</p> <p>3 A. It's -- it's causally</p> <p>4 related or not?</p> <p>5 Q. No, just suggesting</p> <p>6 something is going on.</p> <p>7 A. So it's no causally related</p> <p>8 as this biomarker.</p> <p>9 Q. Okay. Now, if we look at</p> <p>10 your -- the paragraph you wrote, and once</p> <p>11 again, so the record is clear, we're</p> <p>12 looking on Page 5 of your expert report,</p> <p>13 in that paragraph, irrelevance of CA-125,</p> <p>14 you don't have a single reference for any</p> <p>15 of your opinions in that paragraph, do</p> <p>16 you?</p> <p>17 A. Which paragraph, the top</p> <p>18 paragraph?</p> <p>19 Q. Irrelevance of CA-125.</p> <p>20 A. This is general medical</p> <p>21 knowledge. Every medical student will</p> <p>22 know.</p> <p>23 Q. Okay. Doctor --</p> <p>24 A. Every pathologist will know.</p>
<p style="text-align: right;">Page 359</p> <p>1 define. Biomarkers, like serum</p> <p>2 biomarkers, CA-125, has been approved by</p> <p>3 FDA to -- as a biomarker -- this is so</p> <p>4 irrelevant -- to monitor whether the</p> <p>5 tumor come back.</p> <p>6 Q. Doctor, I understand that</p> <p>7 you want to get to that.</p> <p>8 A. That's biomarkers, right?</p> <p>9 Q. Doctor, would you agree that</p> <p>10 a biomarker is a measurable substance in</p> <p>11 an organism whose presence is indicative</p> <p>12 of some phenomenon, such as disease,</p> <p>13 infection or environmental exposure?</p> <p>14 That's a biomarker. Would you agree with</p> <p>15 that?</p> <p>16 A. I need to see your -- what</p> <p>17 you said. I think this is one of the</p> <p>18 definitions.</p> <p>19 Q. Okay. Is it an acceptable</p> <p>20 one to use for our purposes -- our</p> <p>21 discussion right now. Are you</p> <p>22 comfortable with using that?</p> <p>23 A. I have only problem</p> <p>24 indicative. What do you -- what do you</p>	<p style="text-align: right;">Page 361</p> <p>1 Every medical doctor will know.</p> <p>2 Q. Okay.</p> <p>3 A. It's common, common</p> <p>4 knowledge.</p> <p>5 Q. Does that mean that no,</p> <p>6 there's not a reference to the medical</p> <p>7 literature in that paragraph?</p> <p>8 A. This -- there should be</p> <p>9 many. But this is a common sentence. So</p> <p>10 I don't need to reference each one.</p> <p>11 Q. Okay. So it is your -- it</p> <p>12 is your opinion that CA-125 should not be</p> <p>13 considered as indicating the onset or</p> <p>14 heightened risk of the development of</p> <p>15 ovarian cancer, correct?</p> <p>16 A. Definitely is not.</p> <p>17 Q. Okay. I'd like to show you</p> <p>18 a paper we've marked as Exhibit 20 from</p> <p>19 the Journal of Ovarian Research.</p> <p>20 (Document marked for</p> <p>21 identification as Exhibit</p> <p>22 Shih-20.)</p> <p>23 THE WITNESS: Okay. Hold on</p> <p>24 one moment.</p>

<p style="text-align: right;">Page 362</p> <p>1 BY DR. RESTAINO: 2 Q. And this one was 3 published -- we're going back. This one 4 was published ten years ago. 5 A. What. 6 Q. Okay. Now, if you look at 7 the second page. 8 A. Okay. 9 Q. There's a heading there of 10 CA-125 and ovarian cancer. 11 A. CA-125. Yes, I saw that. 12 Q. And do they state there, 13 "The most widely used tumor marker in 14 ovarian cancer, often considered the gold 15 standard is CA-125, Reference 19"? 16 A. Let me see the 19. 17 19 is, okay, cancer antigen 18 125. That's 2008, 11 years ago. 19 Q. Yes. Do you agree that at 20 that time, CA-125 was the most widely 21 used tumor marker in ovarian cancer? 22 MS. MILLER: Objection. 23 THE WITNESS: What do you 24 mean widely used, most widely</p>	<p style="text-align: right;">Page 364</p> <p>1 DR. RESTAINO: The question 2 pending is -- is his 3 interpretation of most widely used 4 tumor marker. 5 MS. MILLER: Do you 6 understand the question that's 7 pending for you? If you 8 understand, great; I don't. 9 THE WITNESS: Okay. Back to 10 the time. And do you have a 11 reference? Let me take a look. 12 BY DR. RESTAINO: 13 Q. Okay. No, we don't have it. 14 A. Oh, you don't have it. 15 Q. No. 16 A. Okay. So you don't have the 17 evidence to show, okay. 18 Then I believe that this is 19 a common belief at that time, back to ten 20 years. 21 Q. Okay. 22 A. Okay. And this is the 23 biomarker for the therapeutic index, but 24 nothing to -- to be related to screening,</p>
<p style="text-align: right;">Page 363</p> <p>1 used? As compared to? 2 BY DR. RESTAINO: 3 Q. That's the language that 4 those researchers use, that it was the 5 most -- what do you -- how do you 6 interpret most widely used? 7 A. Most widely used. Do you 8 have Reference 19? Because this 9 statement is coming from the 19. 10 Q. Correct. 11 A. So I want to see the 12 original articles. Do you have one? 13 Q. Well, no. In the original 14 that underlying article might also 15 reference another article which could 16 reference another article. We're just 17 going by this published article. 18 A. Then... 19 MS. MILLER: Is there a 20 question pending? 21 DR. RESTAINO: It was an 22 answer to his question. 23 MS. MILLER: I'm losing my 24 mind here.</p>	<p style="text-align: right;">Page 365</p> <p>1 early lesions, pathogenesis. It just 2 reflect how many tumor cell you have, how 3 many tumor cell you have. 4 Q. Okay. 5 (Document marked for 6 identification as Exhibit 7 Shih-21.) 8 BY DR. RESTAINO: 9 Q. And I'll hand you what we've 10 now marked as Shih-21. And this paper 11 has been published in the International 12 Journal of Cancer, lead author Kaaks, 13 K-A-A-K-S. It's titled "Tumor-Associated 14 Auto Antibodies As Early Detection 15 Markers For Ovarian Cancer: A 16 prospective evaluation." Published 2018. 17 And this, as the title 18 suggests, was a prospective study, 19 correct? 20 A. I need -- I never see this 21 paper, okay. Let me take some time to 22 read even the title. 23 Q. Doctor, while you are 24 looking at that, look at where your</p>

<p style="text-align: right;">Page 366</p> <p>1 fingers are on the bottom. Do you see 2 the language right underneath your 3 finger? 4 A. Which one? 5 Q. Down at the bottom of the 6 page. 7 A. International Journal of 8 Cancer? 9 Q. No. The -- the language 10 from the journal underneath the -- what's 11 new? 12 A. The box under the what's 13 new? 14 Q. Under the box, yeah. 15 A. Okay. Okay. I have not got 16 there yet, but we can start. 17 Q. Okay. 18 A. You can read to me. 19 Q. Okay. Sir, yeah, I was 20 concerned only because the -- what I -- 21 the only section that I wanted to read to 22 you, I kept noticing your thumb was 23 covering it. 24 A. Thank you very much for your</p>	<p style="text-align: right;">Page 368</p> <p>1 prospective screening? 2 A. Which -- 3 MS. MILLER: Objection. 4 THE WITNESS: Same. I don't 5 know what does that mean, it's too 6 general. What do you mean? 7 BY DR. RESTAINO: 8 Q. What part don't you 9 understand? Do you need different help 10 with prospective or screening? 11 MS. MILLER: Object -- 12 objection. 13 THE WITNESS: Where -- where 14 are you, your prospective term 15 coming from? 16 Could you pinpoint 17 specifically which sentence you 18 are talking about, please? 19 BY DR. RESTAINO: 20 Q. Yes, sir. 21 A. Okay. 22 Q. Down at the bottom. First 23 column on the left, Cancer Antigen-125. 24 A. Yes, I saw that.</p>
<p style="text-align: right;">Page 367</p> <p>1 help. 2 Q. On the -- on the bottom it 3 states, "Cancer Antigen-125 (CA-125) is 4 the best available biomarker for 5 epithelial ovarian cancer, and the only 6 marker tested in prospective screening 7 trials so far." 8 Did I read that correctly? 9 A. That has been said here. 10 Q. Yes. And it -- 11 A. But there is no reference, 12 so I'm surprised. Where is -- is the 13 basis coming from? 14 Q. Okay. Do you have any 15 reason to -- to contradict them when they 16 say it's the best available biomarker for 17 epithelial ovarian cancer? 18 MS. MILLER: Objection. 19 THE WITNESS: This question 20 is too general. I don't know if I 21 can -- 22 BY DR. RESTAINO: 23 Q. Okay. Do you disagree that 24 that's the only marker tested across</p>	<p style="text-align: right;">Page 369</p> <p>1 Q. That's the best available 2 biomarker for epithelial ovarian cancer. 3 Published this year -- excuse me, 2018, 4 correct? 5 A. No. This is -- refer the 6 author's opinion as introduction. This 7 is not based on real result. Okay. 8 Q. Okay. 9 A. So this is a part of 10 introduction. They need to show the 11 readers about why they want to do a 12 study. And there is no citation. So I 13 don't know where this come -- comes from. 14 Q. And there's no citation in 15 your paragraph, in your expert report, 16 where your -- where your contrary 17 conclusions come from, are there -- is 18 there, Doctor? 19 MS. MILLER: Objection. 20 THE WITNESS: Which? 21 MS. MILLER: Objection. 22 BY DR. RESTAINO: 23 Q. Your paragraph in your 24 expert report does not contain a single</p>

<p style="text-align: right;">Page 370</p> <p>1 citation, yet you are criticizing these</p> <p>2 individuals in a peer-reviewed</p> <p>3 publication for the lack of a citation.</p> <p>4 So where is your citation, sir?</p> <p>5 A. Okay. So which part are you</p> <p>6 talking about?</p> <p>7 Q. Your expert report.</p> <p>8 Irrelevance of 125 finding as you</p> <p>9 criticize Dr. Saed. You are putting down</p> <p>10 your subjective opinions in paragraph</p> <p>11 titled "Irrelevance of CA-125 Finding"</p> <p>12 without a citation, correct?</p> <p>13 MR. LOCKE: Objection.</p> <p>14 BY DR. RESTAINO:</p> <p>15 Q. Is it correct? Do you have</p> <p>16 a citation?</p> <p>17 A. They are different. They</p> <p>18 are different. They are different.</p> <p>19 Q. Okay. Now I'd like to show</p> <p>20 you another paper we've marked as</p> <p>21 Shih-22.</p> <p>22 (Document marked for</p> <p>23 identification as Exhibit</p> <p>24 Shih-22.)</p>	<p style="text-align: right;">Page 372</p> <p>1 Detection of Ovarian Cancer" by Elias, et</p> <p>2 al., and this is published in Hematology,</p> <p>3 Oncology Clinics of North America.</p> <p>4 A. Thank you.</p> <p>5 Q. You're welcome.</p> <p>6 A. Early detection.</p> <p>7 Q. Do you remember seeing this</p> <p>8 paper at all, Doctor?</p> <p>9 A. No. This is in a very</p> <p>10 unusual journal. We usually -- as an</p> <p>11 ovarian cancer researcher, we really</p> <p>12 don't read that kind of journals.</p> <p>13 Q. Okay. Are you speaking for</p> <p>14 all ovarian cancer researchers in the</p> <p>15 country?</p> <p>16 A. No, just me. I say me. Of</p> <p>17 course.</p> <p>18 Q. Okay. If you look at the</p> <p>19 key points --</p> <p>20 A. I'm sorry, can I study the</p> <p>21 authors and this and that.</p> <p>22 Q. Sure. Do you know any of</p> <p>23 the authors?</p> <p>24 A. Again, I don't think the</p>
<p style="text-align: right;">Page 371</p> <p>1 BY DR. RESTAINO:</p> <p>2 Q. And, Doctor, the -- your --</p> <p>3 your professional life is all about early</p> <p>4 detection of ovarian cancer, correct?</p> <p>5 MS. MILLER: Objection.</p> <p>6 BY DR. RESTAINO:</p> <p>7 Q. Is that a main part of your</p> <p>8 professional life?</p> <p>9 A. What do you mean</p> <p>10 professional life?</p> <p>11 Q. The work that you do at</p> <p>12 Johns Hopkins?</p> <p>13 A. I diagnose patients' tissues</p> <p>14 as well.</p> <p>15 Q. Yes, I did -- I was -- I did</p> <p>16 not mean to demean all the work that you</p> <p>17 do.</p> <p>18 A. So can you repeat your</p> <p>19 question.</p> <p>20 Q. I'll strike the question.</p> <p>21 MS. MILLER: Why don't we go</p> <p>22 on.</p> <p>23 BY DR. RESTAINO:</p> <p>24 Q. Exhibit Shih-22, "Early</p>	<p style="text-align: right;">Page 373</p> <p>1 authors are important. The scientific</p> <p>2 content is more important for our</p> <p>3 discussion.</p> <p>4 Q. I'm -- okay.</p> <p>5 You asked if you could study</p> <p>6 the authors. So I was just asking if you</p> <p>7 know the authors.</p> <p>8 A. I know the name of Bast.</p> <p>9 Q. Okay. Underneath there, do</p> <p>10 you see the key points for the paper?</p> <p>11 Listed underneath the authors. And</p> <p>12 there's keywords, and then key points.</p> <p>13 Do you see that, sir?</p> <p>14 A. So there are four key</p> <p>15 points.</p> <p>16 Q. Okay. First bullet point</p> <p>17 states, "Given the low prevalence of</p> <p>18 ovarian cancer, even among postmenopausal</p> <p>19 women (1:2,500), an effective screening</p> <p>20 strategy requires high sensitivity</p> <p>21 (greater than 75 percent) and extremely</p> <p>22 high specificity (99.7 percent)."</p> <p>23 Did I read that correctly,</p> <p>24 sir?</p>

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<p style="text-align: right;">Page 374</p> <p>1 A. Yes.</p> <p>2 Q. Do you agree with that</p> <p>3 statement, that an effective screening</p> <p>4 strategy requires high sensitivity,</p> <p>5 extremely high specificity?</p> <p>6 A. So again, I don't know what</p> <p>7 kind of ovarian cancer they are talking</p> <p>8 about because for the detection</p> <p>9 screening, it's so important for the</p> <p>10 histological subtypes.</p> <p>11 Q. And if you can turn to Page</p> <p>12 906.</p> <p>13 A. Okay. Nine -- okay.</p> <p>14 Q. And there's a -- right above</p> <p>15 the Figure 1, there's a heading protein</p> <p>16 biomarkers.</p> <p>17 Do you see that, sir?</p> <p>18 A. Yes.</p> <p>19 Q. And they write, "CA-125</p> <p>20 remains the most sensitive and specific</p> <p>21 protein biomarker for detecting early</p> <p>22 stage disease in apparently healthy</p> <p>23 populations."</p> <p>24 Did I read that correctly?</p>	<p style="text-align: right;">Page 376</p> <p>1 paragraph, to the right of Gonzalez, et</p> <p>2 al. 2016, you start a sentence, "In</p> <p>3 another important study."</p> <p>4 Do you see that, sir?</p> <p>5 A. Yes.</p> <p>6 Q. "In another important study,</p> <p>7 reported by Nicole Urban" -- U-R-B-A-N --</p> <p>8 "et al., based on 74,786 Women's Health</p> <p>9 Initiative (WHI) observational study (OS)</p> <p>10 participants, the authors concluded that</p> <p>11 CA-125 and HE4 contribute significantly</p> <p>12 to a risk prediction classifier combining</p> <p>13 serum markers with epidemiologic risk</p> <p>14 factors. The hybrid risk classifier may</p> <p>15 be useful to identify postmenopausal</p> <p>16 women who would benefit from timely</p> <p>17 surgical intervention to prevent ovarian</p> <p>18 cancer."</p> <p>19 Did I read that correctly,</p> <p>20 sir?</p> <p>21 A. Yes, you did.</p> <p>22 Q. And you described Urban as</p> <p>23 an important study, correct?</p> <p>24 A. I did not cite this as</p>
<p style="text-align: right;">Page 375</p> <p>1 A. It has been written this</p> <p>2 way.</p> <p>3 Q. Okay. And this is a</p> <p>4 publication also in 2018 regarding</p> <p>5 CA-125, correct?</p> <p>6 A. I don't believe this, this</p> <p>7 statement.</p> <p>8 Q. Okay. Now, in your paper,</p> <p>9 you also discuss a paper by Urban, et</p> <p>10 al., U-R-B-A-N.</p> <p>11 Do you recall that name?</p> <p>12 A. Could you show me?</p> <p>13 Q. Yeah, I'll look for it.</p> <p>14 DR. RESTAINO: Jessica has</p> <p>15 much better luck finding these</p> <p>16 things than I do.</p> <p>17 MS. MILLER: You want to</p> <p>18 know where he cites Urban in his</p> <p>19 report?</p> <p>20 DR. RESTAINO: I think I'm</p> <p>21 seeing it.</p> <p>22 BY DR. RESTAINO:</p> <p>23 Q. Yes, on Page 12, top</p> <p>24 paragraph. In the middle of the</p>	<p style="text-align: right;">Page 377</p> <p>1 important study.</p> <p>2 Q. Well, you started off by --</p> <p>3 I started off by reading, "In another</p> <p>4 important study."</p> <p>5 A. Okay.</p> <p>6 Q. Did you -- did you actually</p> <p>7 read the WHI observational study?</p> <p>8 A. I remember that I read that</p> <p>9 before, but when I say important, is</p> <p>10 important in this context, okay.</p> <p>11 It doesn't mean anything</p> <p>12 else. So you need to be careful. When I</p> <p>13 say important, you need to read the whole</p> <p>14 paragraph, and even the entire report to</p> <p>15 know what I say is important. You cannot</p> <p>16 just crop a sentence, one here, there,</p> <p>17 here. That's not fair.</p> <p>18 Q. Okay. Doctor, I can only go</p> <p>19 by the words that you use in your expert</p> <p>20 report.</p> <p>21 Now, if you -- this paper</p> <p>22 that we handed you, Urban, it's</p> <p>23 Exhibit 23, "Identifying Postmenopausal</p> <p>24 Women At Elevated Risk For Epithelial</p>

<p style="text-align: right;">Page 378</p> <p>1 Ovarian Cancer."</p> <p>2 MS. MILLER: Can we have a</p> <p>3 copy?</p> <p>4 (Document marked for</p> <p>5 identification as Exhibit</p> <p>6 Shih-23.)</p> <p>7 BY DR. RESTAINO:</p> <p>8 Q. Doctor, if you turn to the</p> <p>9 second page -- well, first, on the front</p> <p>10 page, this is a 2015 paper, correct?</p> <p>11 A. That's correct.</p> <p>12 Q. So we're not as far back as</p> <p>13 2008, nor are we as current as 2018,</p> <p>14 correct?</p> <p>15 A. Yes.</p> <p>16 Q. And if you turn to Page 254,</p> <p>17 which is the second page, and I'm going</p> <p>18 to try to draw your attention -- left</p> <p>19 paragraph, bottom -- I'm sorry. Left</p> <p>20 column, bottom paragraph, six lines up.</p> <p>21 On the right-hand side, you see CA-125?</p> <p>22 A. Right.</p> <p>23 Q. And they write, "CA-125 is a</p> <p>24 predictive marker for EOC that becomes</p>	<p style="text-align: right;">Page 380</p> <p>1 utilizing that as, in the title,</p> <p>2 epithelial ovarian cancer?</p> <p>3 A. So that would be where?</p> <p>4 Q. Is that your understanding,</p> <p>5 EOC means epithelial ovarian cancer?</p> <p>6 A. That's their definition and</p> <p>7 abbreviation.</p> <p>8 Q. And so they write here that</p> <p>9 "CA-125 is a predictive marker for EOC</p> <p>10 that becomes increasingly sensitive with</p> <p>11 proximity to diagnosis." And then just</p> <p>12 below it in the final sentence, they say,</p> <p>13 "Both CA-125 and HE-4 show promise as</p> <p>14 risk and early detection markers."</p> <p>15 Did I read that correctly?</p> <p>16 A. It has been written in this</p> <p>17 way.</p> <p>18 Q. Okay. And actually there</p> <p>19 they have Reference 16, and then they</p> <p>20 have References 20, 21, 22 and 23. So</p> <p>21 they have five references to support that</p> <p>22 statement, correct?</p> <p>23 A. It depends on what -- what</p> <p>24 kind of references. Good or bad. I need</p>
<p style="text-align: right;">Page 379</p> <p>1 increasingly sensitive with proximity to</p> <p>2 disease."</p> <p>3 Doctor, what is meant by</p> <p>4 EOC?</p> <p>5 A. This is not a regularly used</p> <p>6 term in ovarian cancer community. So I</p> <p>7 need to figure out what is their</p> <p>8 definition.</p> <p>9 Q. Well, Doctor, this paper is</p> <p>10 published in Gynecologic Oncology.</p> <p>11 And is it your opinion that</p> <p>12 oncologists and gynecological</p> <p>13 pathologists don't know what EOC stands</p> <p>14 for?</p> <p>15 MS. MILLER: Objection.</p> <p>16 THE WITNESS: Different --</p> <p>17 MS. MILLER: Objection.</p> <p>18 THE WITNESS: Different</p> <p>19 groups of people using different</p> <p>20 abbreviations. So this is a</p> <p>21 private abbreviation.</p> <p>22 BY DR. RESTAINO:</p> <p>23 Q. Okay. Do you understand</p> <p>24 when they use EOC here that they are</p>	<p style="text-align: right;">Page 381</p> <p>1 to see them. Okay. 16.</p> <p>2 Do you have those</p> <p>3 references, that would be wonderful for</p> <p>4 the discussion. By looking at the title</p> <p>5 I don't know the science quality inside</p> <p>6 this paper.</p> <p>7 Q. Okay. Do you have any</p> <p>8 reason to believe that this paper in</p> <p>9 Gynecologic Oncology is misrepresenting</p> <p>10 what the references state?</p> <p>11 MR. LOCKE: Objection.</p> <p>12 THE WITNESS: I don't know</p> <p>13 how they interpret their reading</p> <p>14 and the interpretation. So I</p> <p>15 cannot answer that question.</p> <p>16 That's their written, that's their</p> <p>17 opinion, it's not my opinion.</p> <p>18 BY DR. RESTAINO:</p> <p>19 Q. Okay. I see. Okay. So,</p> <p>20 Doctor, it was okay for you to rely upon</p> <p>21 this paper, and for you to cite this</p> <p>22 paper in your expert report as an</p> <p>23 important study when you were discussing</p> <p>24 it in your expert report, but now in your</p>

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<p style="text-align: right;">Page 382</p> <p>1 deposition, now you can't rely upon 2 anything that's published in this paper? 3 MS. MILLER: Objection. 4 MR. LOCKE: Objection. 5 MS. MILLER: That's not what 6 he said. You are misstating his 7 testimony. 8 If you -- would you like to 9 explain? 10 THE WITNESS: Okay. 11 So you just tell me in the 12 introduction, you crop the couple 13 of sentences and ask me about the 14 opinion. 15 But you know how many 16 sentences in this article? You 17 don't know, right? Many. 18 BY DR. RESTAINO: 19 Q. No. But I do know that 20 you've quoted two sentences in your 21 expert report from this sentence -- from 22 this paper. 23 A. Okay. Let me -- let me go 24 back and make sure.</p>	<p style="text-align: right;">Page 384</p> <p>1 Q. Okay. 2 A. In -- in terms of CA-125 as 3 a biomarker is not relevant to talcum 4 powder at all. Biomarker is just a 5 serum -- is just a circulating proteins. 6 It doesn't mean that is important for 7 normal fallopian tube epithelium cells, 8 to become p53 signature or STIC. So it's 9 not totally relevant. 10 In early detection is a 11 biomarker association does not mean there 12 is a causal relationship. 13 Q. Okay. 14 (Document marked for 15 identification as Exhibit 24.) 16 BY DR. RESTAINO: 17 Q. Doctor, one more paper in 18 this area. You may recognize the title. 19 "Critical Questions in Ovarian Cancer 20 Research in Treatment: Report of the 21 American Association For Cancer Research 22 special conference." 23 Does that sound familiar to 24 you, sir?</p>
<p style="text-align: right;">Page 383</p> <p>1 Q. Sure. 2 MS. MILLER: We are at 3 exactly five hours. Do you want 4 to take a break now? 5 DR. RESTAINO: I -- I do. 6 MS. MILLER: Six hours. I'm 7 sorry, six hours. I just thought 8 maybe this would be a good time 9 for a last break. 10 DR. RESTAINO: Sure. One 11 more paper to go through and we'll 12 take a break. 13 THE WITNESS: Okay. All 14 right. 15 The -- okay. Can I start? 16 BY DR. RESTAINO: 17 Q. Yeah, sure. 18 A. So the purpose I cite this 19 paper -- 20 Q. Yes. 21 A. -- is to show that talc use 22 did not carry any significant -- or any 23 risk for ovarian cancer. That's my 24 purpose.</p>	<p style="text-align: right;">Page 385</p> <p>1 A. I need to see it. 2 Q. Sure. 3 A. Yes, I'm one of the 4 co-authors. 5 Q. That you are. 6 A. Yes. 7 Q. And if you look at the 8 bottom of the first page. Very, very 9 bottom, in the tiny little print, all the 10 way down at the bottom, it says, 11 "Received August 24, 2018. Revised 12 December 17, 2018. Accepted 2019. And 13 published online month 00 2019." 14 So this is a very current 15 paper, correct? 16 A. I agree. 17 Q. Okay. And, Doctor, did you 18 have any part to -- to play in the 19 revised version that was submitted on 20 December 17, 2018? 21 A. To be honest, I am on this 22 as a co-author, because we participate in 23 a meeting. And this is like a meeting 24 report. So everybody talk about things,</p>

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<p style="text-align: right;">Page 386</p> <p>1 and so Dr. Bast, the first author as you 2 can see here, the CA-125 discover person, 3 and he write -- I think probably he wrote 4 this paper by summarizing our opinion 5 during the conference -- conference. 6 Okay? 7 So after that, I did not see 8 the revision and this and that. So I am 9 participating in this as a co-author, 10 because I contribute to the discussion 11 during the -- during the symposium of 12 ovarian cancer. 13 Q. Okay. If you -- if you turn 14 to Page 8 of this paper? 15 A. 8? 16 Q. Yes, sir. 17 A. Okay. Yes. 18 Q. And on the right side where 19 there's conflict of interest disclosure, 20 your name is not listed, correct? Were 21 you a retained expert for Johnson & 22 Johnson while you were engaged in this 23 process? 24 A. I think this is way before I</p>	<p style="text-align: right;">Page 388</p> <p>1 BY DR. RESTAINO: 2 Q. Okay. So, Doctor, 3 reasonable scientists can reasonably 4 disagree, correct? 5 MS. MILLER: Objection. 6 Vague. 7 THE WITNESS: It's too 8 vague. What's your question? 9 BY DR. RESTAINO: 10 Q. Okay. While you are 11 disagreeing with Dr. Saed's use of CA-125 12 and I've now shown you four papers 13 supporting the use of CA-125 including a 14 2019 paper for which you are a co-author. 15 MS. MILLER: Objection. 16 Those papers did not use CA-125 in 17 the same way as Dr. Saed. That is 18 such a disingenuous question. 19 MS. PARFITT: It's objection 20 to form. 21 BY DR. RESTAINO: 22 Q. Doctor, can reasonable 23 scientists reasonably disagree? 24 MS. MILLER: Objection.</p>
<p style="text-align: right;">Page 387</p> <p>1 am involved in this litigation. 2 Q. Okay. Now, if you -- on the 3 left column, that's a section called 4 "Conclusions," correct? 5 A. Correct. 6 Q. And in this paper that was 7 published in 2019, this group including 8 yourself write, "In answering these 9 'critical questions,' we have learned 10 that screening algorithms measuring the 11 trend of CA-125 values over time can 12 achieve adequate specificity, but we must 13 improve the sensitivity of panels of 14 biomarkers for early detection of ovarian 15 cancer, possibly utilizing 16 autoantibodies, antigen-autoantibody 17 complexes, and nucleic acid." 18 Did I read that correctly? 19 MS. MILLER: Objection. 20 THE WITNESS: I think this 21 is Dr. Bast's opinion, because 22 that's his research field exactly. 23 And he is the author who wrote 24 this paper.</p>	<p style="text-align: right;">Page 389</p> <p>1 THE WITNESS: No. It's 2 based on biological plausibility 3 and the specific question you want 4 answered. 5 I'm asking, or we are 6 addressing the early STIC and p53 7 signature in the fallopian tube, 8 whether talc can cause ovarian 9 cancer and cause the precursor. 10 Now, you are diverting the 11 discussion into the CA-125. And 12 CA-125 is a biomarker for 13 monitoring disease for -- this is 14 well known. 15 So I don't know why this 16 question is relevant. And this 17 is -- should be not existent. 18 BY DR. RESTAINO: 19 Q. So when you disagree that 20 CA-125 is a clinically irrelevant 21 biomarker for ovarian cancer, you 22 disagree with the authors that we've just 23 discussed, right? 24 MR. LOCKE: Objection.</p>

<p style="text-align: right;">Page 390</p> <p>1 MS. MILLER: Objection. I'm 2 sorry. 3 THE WITNESS: Okay. 4 BY DR. RESTAINO: 5 Q. Go back to the paragraph in 6 your expert report. "Irrelevance of 7 CA-125," the final sentence, "Thus 8 Dr. Saed's statement in the conclusion of 9 the report that CA-125 is 'clinically 10 relevant biomarker for ovarian 11 cancer'" -- and there's your reference -- 12 "is misleading and data from CA-125 are 13 not relevant to support the research and 14 conclusion." 15 A. I'm sorry. Where are you? 16 Which page? 17 Q. I'm sorry. Page 5. 18 A. Right. 19 Q. The paragraph -- second 20 paragraph from the bottom, "Irrelevance 21 of CA-125 Findings." 22 A. Oh, I know what's that. So 23 you need to be careful for the context. 24 So why I want to say that is</p>	<p style="text-align: right;">Page 392</p> <p>1 mischaracterizing his testimony. 2 MS. PARFITT: It's 3 "objection to form." 4 MS. MILLER: And as I said, 5 you are mischaracterizing how 6 Dr. Saed uses CA-125. 7 THE WITNESS: Right. You 8 should read Dr. Saed paper. 9 BY DR. RESTAINO: 10 Q. Sir, I'm reading your expert 11 report in your language. 12 A. My language is referring to 13 Dr. Saed's. You see here my opinion 14 about Dr. Saed's. So we need to go back 15 to Dr. Saed's paper. And we can discuss. 16 How about that? 17 Q. I'm just going by what 18 you've stated in your expert report. 19 DR. RESTAINO: We can take 20 our break now. 21 THE WITNESS: Okay. Sure. 22 THE VIDEOGRAPHER: The time 23 is 4:56 p.m. We're going off the 24 record.</p>
<p style="text-align: right;">Page 391</p> <p>1 irrelevant of why we are discuss. That's 2 why we want to bring the discussion 3 relevant here. 4 What I say here is Dr. Saed 5 treat ovarian cancer cell line which is 6 total incorrect methodology, with talcum 7 powder, Johnson & Johnson powder, and 8 took CA-125. Then he misrepresented, 9 totally wrong that CA-125 because of the 10 increased CA-125, that talcum powder is a 11 carcinogen, which is totally incorrect, 12 in this specific context. 13 So don't -- you need to be 14 careful about what you are referring to. 15 Q. When Dr. Saed states that 16 CA-125 is a, "Clinically relevant 17 biomarker for ovarian cancer," he is not 18 being misleading, for we've just read 19 four papers, including one by yourself, 20 that supports the use, between 2008 and 21 2019, the use of CA-125 for the early 22 detection of ovarian cancer, correct? 23 MR. LOCKE: Objection. 24 MS. MILLER: That's again</p>	<p style="text-align: right;">Page 393</p> <p>1 (Short break.) 2 THE VIDEOGRAPHER: The time 3 is 5:14 p.m. We are back on the 4 record. 5 BY DR. RESTAINO: 6 Q. Doctor, looking at your 7 expert report, please, on the bottom of 8 Page 5, you have a paragraph there which 9 goes over to 6 titled "Extrapolation From 10 an In Vivo Experiment," correct? 11 A. What I meant is -- let me 12 see. 13 MS. MILLER: Are you just 14 asking if those words are there? 15 DR. RESTAINO: Just 16 directing him to that area. 17 MS. MILLER: Page 5. 18 DR. RESTAINO: Page 5 going 19 over to Page 6. 20 MS. MILLER: Oh, okay. 21 BY DR. RESTAINO: 22 Q. Do you see that, Doctor? 23 A. Yes. 24 Q. And actually, you started</p>

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<p style="text-align: right;">Page 394</p> <p>1 off by saying, "What I meant is." 2 Doctor, what did you mean in that 3 paragraph? 4 A. I expressed my opinion about 5 Dr. Saed's claims in his summary 6 paragraph. And what he said, this is 7 very important. 8 "This study has shown a 9 dose-dependent significant increase in 10 key pro-oxidants and concomitant increase 11 in key anti-oxidant enzymes in all talc 12 retreated cells, both normal and ovarian 13 cancer, compared to their control." 14 But we know this is in vitro 15 study. 16 What I mean is they don't 17 have any in vivo support, because 18 carcinogen, I think that's -- if you 19 agree, that's the main things about the 20 talcum powder issue. 21 So the carcinogen based on 22 the definition from the dictionary or 23 NCI, is the chemical compounds, reagents 24 that can cause cancer, and of course</p>	<p style="text-align: right;">Page 396</p> <p>1 conduct an in vitro study, determine the 2 results of that study, and based upon the 3 results, perhaps then say, now let's do 4 an in vivo study and see if we see this 5 in animals. And if so, and it's perhaps 6 a treatment, now let's do a Phase I 7 study, clinical study, and find out the 8 dose or the safety parameters, and based 9 upon that, do a Phase II study, and based 10 upon that do a Phase III study. And 11 perhaps in some cases even a Phase IV 12 postmarketing study. 13 So that from in vitro to 14 Phase IV is not uncommon in science 15 research, correct? 16 MS. MILLER: Objection. 17 THE WITNESS: You are 18 talking about general science? 19 BY DR. RESTAINO: 20 Q. Yes, sir. 21 A. So general science -- 22 Q. Yes, sir? 23 A. -- cannot apply to the 24 individual ones.</p>
<p style="text-align: right;">Page 395</p> <p>1 cancer meaning from a tissue. So they 2 did not show any evidence biologically 3 plausible evident that talcum powder 4 is -- can cause ovarian cancer. 5 This -- everything is just 6 in vitro evidence. 7 Q. Yes, and in vitro means in 8 essence either looking at a slide or a 9 petri dish, correct? 10 A. No. Slide is human tissue. 11 I think that's a tissue study. In vitro 12 meaning -- we need to be careful here. 13 We need to define this very well. In 14 vitro meaning not inside animal tissue or 15 human tissues. Everything is based on 16 cell culture in petri dish, and you add 17 the drug in the condition, 18 un-physiologically high concentration. 19 And you measure the proliferation, 20 apoptosis, and that is exactly what 21 Dr. Saed did. 22 Q. Okay. Now, Doctor, to be 23 fair, in scientific research, it is not 24 uncommon for a person or a team to</p>	<p style="text-align: right;">Page 397</p> <p>1 For example, in this case, 2 if we want to test talcum powder is 3 carcinogenic at all, this kind of lousy 4 science is not helpful at all. They -- 5 they are just end -- without quotes, 6 without evidence, cultured evidence to 7 show anything biologically meaningful and 8 any mechanism. It's just in vitro. And 9 Dr. Saed -- go ahead. 10 Q. Okay. Okay. Well, as you 11 write, the significance of the finding is 12 unclear. 13 Well, the significance of 14 every finding becomes clearer and clearer 15 as we step up in the different studies. 16 In vitro to in vivo or animal, to human 17 testing, correct? 18 A. This depends on your in 19 vitro study, how solid it is. How much 20 biological plausibility it can offer. So 21 if this is the case, then people will 22 be -- love to test in vivo, in human 23 trial. But in the first phase, like 24 Saed's paper, they are filled with a lot</p>

<p style="text-align: right;">Page 398</p> <p>1 of problems and the wrong methodologies.</p> <p>2 I don't think any people</p> <p>3 will look at this paper and will carry</p> <p>4 any meaningful significance biologically</p> <p>5 to them.</p> <p>6 Q. You're purely speculating on</p> <p>7 what other readers are going to take away</p> <p>8 from this paper, aren't you?</p> <p>9 MS. MILLER: Objection.</p> <p>10 Objection.</p> <p>11 THE WITNESS: Which readers?</p> <p>12 Can you pinpoint which readers?</p> <p>13 BY DR. RESTAINO:</p> <p>14 Q. Any reader. When you say</p> <p>15 that, "I don't think any people will look</p> <p>16 at this paper," what people were you</p> <p>17 talking about?</p> <p>18 MS. MILLER: Objection.</p> <p>19 That's --</p> <p>20 MS. PARFITT: "Objection to</p> <p>21 form" is fine.</p> <p>22 MS. MILLER: Thank you,</p> <p>23 Michelle.</p> <p>24 MS. PARFITT: You're</p>	<p style="text-align: right;">Page 400</p> <p>1 correct?</p> <p>2 MS. MILLER: Objection.</p> <p>3 BY DR. RESTAINO:</p> <p>4 Q. There's nothing</p> <p>5 inappropriate about that?</p> <p>6 MS. MILLER: Objection.</p> <p>7 THE WITNESS: I answer your</p> <p>8 question already.</p> <p>9 BY DR. RESTAINO:</p> <p>10 Q. Okay. Doctor, do you have</p> <p>11 an opinion on whether the talcum powder</p> <p>12 products that we are discussing in this</p> <p>13 case contain asbestos?</p> <p>14 MS. MILLER: Objection.</p> <p>15 THE WITNESS: I don't know.</p> <p>16 BY DR. RESTAINO:</p> <p>17 Q. Okay. Do you have an</p> <p>18 opinion as to whether the talcum powder</p> <p>19 products at issue in this case ever</p> <p>20 contained asbestos?</p> <p>21 MS. MILLER: Objection.</p> <p>22 THE WITNESS: I don't know.</p> <p>23 BY DR. RESTAINO:</p> <p>24 Q. Do you have an opinion on</p>
<p style="text-align: right;">Page 399</p> <p>1 welcome.</p> <p>2 THE WITNESS: People. What</p> <p>3 do you mean people? Where I said</p> <p>4 people, right? That's why --</p> <p>5 BY DR. RESTAINO:</p> <p>6 Q. Can we agree that --</p> <p>7 MS. MILLER: You read back</p> <p>8 only half the sentence. That's --</p> <p>9 BY DR. RESTAINO:</p> <p>10 Q. Doctor, can we agree that</p> <p>11 there's no --</p> <p>12 A. Can I see that?</p> <p>13 Okay. The people here means</p> <p>14 the scientists who really read this</p> <p>15 paper, and I'm very sure they will still</p> <p>16 agree that this is really shocking paper</p> <p>17 to them, because there is no -- this is</p> <p>18 just like a script by some other party</p> <p>19 for litigation purpose.</p> <p>20 Q. But, Doctor, it's not</p> <p>21 inappropriate to look at the results of</p> <p>22 an in vitro study, and then based upon</p> <p>23 those results, do the next study in line,</p> <p>24 perhaps an in vivo or animal study,</p>	<p style="text-align: right;">Page 401</p> <p>1 whether the talcum powder products at</p> <p>2 issue in this case contain fibrous talc</p> <p>3 also known as talc in an asbestiform</p> <p>4 habit?</p> <p>5 MS. MILLER: Objection.</p> <p>6 Foundation.</p> <p>7 THE WITNESS: This is beyond</p> <p>8 my expertise and you should ask</p> <p>9 mineralogist and a toxicologist,</p> <p>10 geologist.</p> <p>11 BY DR. RESTAINO:</p> <p>12 Q. Does that -- I'm sorry.</p> <p>13 Does that mean you don't have an opinion?</p> <p>14 A. I already answered my</p> <p>15 question.</p> <p>16 Q. Okay. Do you have an</p> <p>17 opinion on whether the talcum powder</p> <p>18 products at issue in this case contain --</p> <p>19 ever contained fibrous talc, also known</p> <p>20 as talc in an asbestiform habit?</p> <p>21 MS. MILLER: Objection.</p> <p>22 THE WITNESS: Same answer to</p> <p>23 that previous question.</p> <p>24 BY DR. RESTAINO:</p>

Page 402	Page 404
<p>1 Q. Do you have an opinion on 2 whether asbestos is a known carcinogen? 3 MS. MILLER: Objection. 4 THE WITNESS: I did not 5 study asbestos. 6 BY DR. RESTAINO: 7 Q. Do you have an opinion on 8 whether fibrous talc is a known 9 carcinogen? 10 A. I did not study it either. 11 Q. Do you have an opinion on 12 whether asbestos can cause ovarian 13 cancer? 14 A. There is no credible science 15 and cogent evidence. If you have one, 16 please show it to me. 17 Q. Do you have an opinion on 18 whether fibrous talc, also known as talc 19 in an asbestiform habit, can cause 20 ovarian cancer? 21 MS. MILLER: Object to form. 22 I think you already asked 23 this. 24 THE WITNESS: You asked me</p>	<p>1 THE WITNESS: No. 2 MS MILLER: That's not what 3 he said. 4 THE WITNESS: No. 5 BY DR. RESTAINO: 6 Q. I'll rephrase it. Do you 7 have an opinion as to whether your 8 opinions in this case are limited to 9 talcum powder products that do not 10 contain asbestos or fibrous talc? 11 MS. MILLER: Objection. 12 MS. SHARKO: I don't 13 understand the question. 14 MS. MILLER: That's just an 15 incomprehensible question. 16 THE WITNESS: Could you ask 17 a question that is easily 18 understood? The limitation was 19 limited. 20 BY DR. RESTAINO: 21 Q. Do your opinions in this 22 case -- are your opinions in this case 23 limited to talc, talcum powder products, 24 which do not contain asbestos?</p>
Page 403	Page 405
<p>1 several times. 2 BY DR. RESTAINO: 3 Q. No. 4 A. Same answer. 5 Q. Okay. And do you have an 6 opinion -- so your opinions in this case, 7 is it fair to say, are limited to talcum 8 powder products that do not contain 9 asbestos or fibrous talc? 10 A. I cannot -- 11 MS. MILLER: Objection. No, 12 that is not what he said. 13 THE WITNESS: No. 14 MS. PARFITT: Objection to 15 form is fine. Jessica, don't 16 coach the witness. 17 MS. MILLER: He can't -- I'm 18 not coaching the witness. He's 19 mischaracterizing his testimony. 20 MS. PARFITT: He asked a 21 question, asked an opinion. He 22 said do you have an opinion. 23 MS. MILLER: No, he said 24 it's fair --</p>	<p>1 MS. MILLER: Objection. 2 THE WITNESS: So are you 3 asking me whether this talc, 4 talcum powder products contain 5 asbestos? 6 BY DR. RESTAINO: 7 Q. No, sir. 8 A. But that's what you ask -- 9 you are asking me. 10 Q. No, I'm asking you if your 11 opinions in this case are limited to the 12 evaluation of talcum powder products 13 which do not contain asbestos. 14 MS. MILLER: Again, I'm 15 going to object to that question. 16 I think it's misleading. I think 17 it's confusing. And I -- he said 18 his opinions are related -- 19 THE WITNESS: Okay. I'm 20 here as expert to express my 21 opinion on whether talcum powder 22 can cause ovarian cancer. And 23 also I bring up the issue of 24 Dr. Saed's paper, which is</p>

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<p>1 really -- emperor has no clothes. 2 There's no evidence. That is my 3 position here today. 4 DR. RESTAINO: Move to 5 strike as unresponsive. 6 BY DR. RESTAINO: 7 Q. Doctor, did you assume for 8 purposes of your opinions today that 9 talcum powder products do not contain 10 asbestos? 11 MS. MILLER: Objection. 12 Asked and answered in a 13 different -- with different 14 wording. And I feel like 15 you're -- 16 MS. PARFITT: Objection to 17 form. 18 MS. MILLER: -- trying to 19 confuse the witness because he's 20 not -- 21 MS. PARFITT: Object to 22 form. 23 MS. MILLER: Because he 24 doesn't have English as his first</p>	<p>1 to help you? Because I can 2 easily. 3 DR. RESTAINO: Sure. 4 MS. SHARKO: Dr. Shih was 5 asked to assume talcum powder is 6 what it is in the container and he 7 was not asked to address asbestos 8 or heavy metals or fragrances or 9 all that. Just whatever the 10 talcum powder is. 11 MS. PARFITT: That's not 12 your question. 13 DR. RESTAINO: Yeah, yeah. 14 Truthfully that's not my question. 15 MS. PARFITT: Thank you, 16 Susan. I appreciate that. 17 MS. MILLER: That is exactly 18 your question. You asked him what 19 was -- 20 MS. SHARKO: Then ask the 21 question. 22 MR. LOCKE: Yeah, that's -- 23 MS. PARFITT: Michelle, 24 Could you please.</p>
Page 407	Page 409
<p>1 language. 2 DR. RESTAINO: Your expert. 3 MS. MILLER: So what? 4 DR. RESTAINO: So if he 5 can't understand English that's 6 not my problem. 7 MS. MILLER: No, it's not 8 that he can't understand. It's 9 that you are asking very confusing 10 questions and repeating the same 11 questions in multiple different 12 ways in an attempt to confuse him. 13 MS. PARFITT: Counsel, 14 object to form. Please. We're 15 almost done. 16 THE WITNESS: Okay. So I'm 17 so distracted. So could you ask 18 one more time in a way that you 19 think I will understand? 20 MS. SHARKO: Do you want -- 21 do you want me to help you, 22 Mr. Restaino -- 23 DR. RESTAINO: Sure. 24 MS. SHARKO: Do you want me</p>	<p>1 (Whereupon, the court 2 reporter read back the requested 3 portion of testimony.) 4 MS. MILLER: Objection. 5 Asked and answered. 6 THE WITNESS: I already 7 answered that in the very 8 beginning. 9 MS. PARFITT: Could you 10 repeat your answer? 11 THE WITNESS: I already 12 answered. 13 BY DR. RESTAINO: 14 Q. But what is your answer? 15 A. You can see in the 16 transcript. 17 Q. It's your assumption that 18 the talcum powder does not contain 19 asbestos? 20 MS. MILLER: Objection. 21 BY DR. RESTAINO: 22 Q. Was that your answer? 23 MS. MILLER: Objection. 24 THE WITNESS: I already</p>

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<p style="text-align: right;">Page 410</p> <p>1 answered.</p> <p>2 BY DR. RESTAINO:</p> <p>3 Q. Doctor, are your opinions in</p> <p>4 this case limited to talcum powder</p> <p>5 products that do not contain fibrous</p> <p>6 talc?</p> <p>7 MS. MILLER: Objection.</p> <p>8 THE WITNESS: So based on my</p> <p>9 literature search and the Saed's</p> <p>10 paper, I reviewed those studies</p> <p>11 using talcum powder and the</p> <p>12 Johnson & Johnson's products in</p> <p>13 all the epidemiology research and</p> <p>14 the Saed research, in animal</p> <p>15 studies.</p> <p>16 That's -- that's my</p> <p>17 knowledge about this talcum</p> <p>18 powder.</p> <p>19 BY DR. RESTAINO:</p> <p>20 Q. Okay. Doctor, have you</p> <p>21 heard a term "biologic plausibility"?</p> <p>22 A. Yes.</p> <p>23 Q. And what does that mean to</p> <p>24 you?</p>	<p style="text-align: right;">Page 412</p> <p>1 were premarked earlier this</p> <p>2 morning. And we went -- I went</p> <p>3 out of my chronological plan.</p> <p>4 MS. MILLER: Okay.</p> <p>5 BY DR. RESTAINO:</p> <p>6 Q. Doctor, this is a paper --</p> <p>7 MS. MILLER: Do we have a</p> <p>8 copy?</p> <p>9 DR. RESTAINO: Oh, I didn't</p> <p>10 give it to you.</p> <p>11 MS. MILLER: I don't think I</p> <p>12 got one.</p> <p>13 BY DR. RESTAINO:</p> <p>14 Q. This is a paper titled</p> <p>15 "Papillary Tubal Hyperplasia: The</p> <p>16 Putative Precursor of Ovarian Atypical</p> <p>17 Proliferative (Borderline) Serous Tumors,</p> <p>18 Non-Invasive Implants, and</p> <p>19 Endosalpingosis."</p> <p>20 E-N-D-O-S-A-L-P-I-N-G-O-S-I-S.</p> <p>21 Lead author is Robert J.</p> <p>22 Kurman, correct?</p> <p>23 A. Yes.</p> <p>24 Q. And last named author is</p>
<p style="text-align: right;">Page 411</p> <p>1 A. I think I said that in the</p> <p>2 morning, probably forgot, that's fine. I</p> <p>3 can say that one more time.</p> <p>4 Biological plausibility</p> <p>5 means credible science, cogent evidence</p> <p>6 to support the biological plausibility of</p> <p>7 statement. In this statement, is the</p> <p>8 talcum powder induced ovarian cancer.</p> <p>9 And I don't find any biological</p> <p>10 plausibility in this case.</p> <p>11 (Document marked for</p> <p>12 identification as Exhibit</p> <p>13 Shih-12.)</p> <p>14 DR. RESTAINO: Michelle, can</p> <p>15 we go ahead and mark this -- oh,</p> <p>16 it's already been marked. Forgive</p> <p>17 me. I'm sorry.</p> <p>18 BY DR. RESTAINO:</p> <p>19 Q. Shih-12.</p> <p>20 MS. MILLER: I'm confused.</p> <p>21 How do you have it if you've</p> <p>22 already marked it?</p> <p>23 MS. PARFITT: Premarked.</p> <p>24 DR. RESTAINO: Because they</p>	<p style="text-align: right;">Page 413</p> <p>1 yourself, correct?</p> <p>2 A. I am.</p> <p>3 Q. And this is published in the</p> <p>4 American Journal of Surgical Pathology in</p> <p>5 2011, correct?</p> <p>6 A. Yes.</p> <p>7 Q. And if you look down at the</p> <p>8 very, very last line in the abstract on</p> <p>9 the front page, you see, you and</p> <p>10 Dr. Kurman, et al., write, "We propose a</p> <p>11 model for the development of ovarian and</p> <p>12 extraovarian low grade serous</p> <p>13 proliferations (APST, non-invasive</p> <p>14 epithelial implants and endosalpingosis)</p> <p>15 that postulates that all of these lesions</p> <p>16 are derived from PTH, which appears to be</p> <p>17 induced by chronic inflammation. If this</p> <p>18 hypothesis is confirmed, then it can be</p> <p>19 concluded that low and high grade ovarian</p> <p>20 tumors develop from tubal epithelium and</p> <p>21 involve the ovary secondarily."</p> <p>22 Did I read that correctly?</p> <p>23 A. Correct.</p> <p>24 Q. Doctor, in 2011 was it</p>

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<p style="text-align: right;">Page 414</p> <p>1 biologically plausible that chronic 2 inflammation would initiate this 3 pathology? 4 A. Say that one more time. 5 Q. In 2011, when you and 6 Dr. Kurman, et al., wrote this paper, was 7 it biologically plausible that chronic 8 inflammation would initiate this 9 pathology? 10 MS. MILLER: Which 11 pathology? 12 DR. RESTAINO: The pathology 13 that I just read about, described 14 in his paper. 15 MS. MILLER: Objection. 16 THE WITNESS: This paper 17 presents our hypothesis in 2011. 18 So how can science advances? 19 It is because we have different 20 findings, come out with 21 hypothesis, or just generate 22 hypothesis from nowhere. 23 Then scientists can decide 24 to test this hypothesis using the</p>	<p style="text-align: right;">Page 416</p> <p>1 So again, this is a 2 hypothesis. 3 BY DR. RESTAINO: 4 Q. Did you think that your 5 hypothesis was biologically plausible? 6 MS. MILLER: Objection. 7 THE WITNESS: I already say 8 that. Biological plausibility 9 should be more than hypothesis. 10 BY DR. RESTAINO: 11 Q. If you turn to Page 8 of 12 this paper, sir, in the second paragraph, 13 it starts on, "Based on the findings in 14 this study." 15 Do you see that, sir? 16 A. Which page? 17 Q. Page 8. 18 A. Okay. Here you go. 19 Q. Yeah. 20 A. And which paragraph? 21 Q. Second paragraph. 22 A. Okay. 23 MS. MILLER: First full 24 paragraph?</p>
<p style="text-align: right;">Page 415</p> <p>1 correct methodologies to prove or 2 to provide biological plausibility 3 of this hypothesis. So that's 4 what we meant here. 5 BY DR. RESTAINO: 6 Q. Okay. But you would not 7 develop, nor would Dr. Kurman, a 8 hypothesis that wasn't based on 9 biological plausibility, would you? 10 MS. MILLER: Objection. 11 THE WITNESS: Can you say 12 that one more time. 13 BY DR. RESTAINO: 14 Q. You would not develop, nor 15 would Dr. Kurman, a hypothesis that 16 wasn't based on biological plausibility? 17 MS. MILLER: Objection. 18 THE WITNESS: Okay. 19 Biological plausibility should be 20 more than hypothesis. And this is 21 a hypothesis awaiting for 22 proven -- not proven -- to support 23 it by credible science in the 24 future.</p>	<p style="text-align: right;">Page 417</p> <p>1 BY DR. RESTAINO: 2 Q. First full paragraph. It 3 says, "Based on the findings in this 4 study." 5 Do you see that, sir? 6 A. Yes. 7 Q. Okay. "Based on the 8 findings of this study, we propose the 9 following model for the origin and 10 development of the entire spectrum of 11 pelvic low grade serous proliferations. 12 Chronic inflammation induces a 13 proliferation of tubal epithelium that 14 could progress to PTH in some women." 15 Doctor, in 2011 when you 16 wrote this, was it biologically plausible 17 for chronic inflammation to induce 18 proliferation of tubal epithelium? 19 MS. MILLER: Objection. 20 THE WITNESS: As we state -- 21 so the answer is no. What we say, 22 we propose it. We hypothesize 23 this model for future scientists 24 or pathologists to test. You have</p>

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<p style="text-align: right;">Page 418</p> <p>1 seen the right methodology. And</p> <p>2 to provide, like, for instance a</p> <p>3 mouse study, et cetera. I don't</p> <p>4 want to deliberate here too much.</p> <p>5 This is hypothesis, for the</p> <p>6 future biological plausibility to</p> <p>7 provide the evidence.</p> <p>8 So this is a hypothesis.</p> <p>9 And again, there's many</p> <p>10 hypothesis. I said this many</p> <p>11 times.</p> <p>12 Biological plausibility</p> <p>13 should be more than hypothesis.</p> <p>14 You need to have credible science</p> <p>15 and a cogent evidence to support.</p> <p>16 BY DR. RESTAINO:</p> <p>17 Q. So, Doctor, on the bottom</p> <p>18 paragraph, of this, on the same page that</p> <p>19 starts, "In conclusion," in the third</p> <p>20 line down, you have a sentence that</p> <p>21 starts, "The process begins with chronic</p> <p>22 inflammation, leading to tubal</p> <p>23 hyperplasia, which, if it progresses to</p> <p>24 PTH, can shed and implant tubal</p>	<p style="text-align: right;">Page 420</p> <p>1 carcinoma, we have a -- the mouse study,</p> <p>2 we put a TP53 mutation into the mullerian</p> <p>3 epithelial cells. And they develop STIC</p> <p>4 and they become cancer.</p> <p>5 Q. Okay. Doctor --</p> <p>6 A. And that's the cancer cell</p> <p>7 reports for several years ago. And</p> <p>8 that's the best evidence.</p> <p>9 Q. After this paper was</p> <p>10 published --</p> <p>11 A. Right.</p> <p>12 Q. -- did you alone or with</p> <p>13 Dr. Kurman or anyone else test the</p> <p>14 hypothesis to determine whether -- when</p> <p>15 the process begins with chronic</p> <p>16 inflammation, if it did, in fact, lead to</p> <p>17 ultimately the development of low grade</p> <p>18 and high grade serous epithelial tumors?</p> <p>19 MS. MILLER: Objection. I</p> <p>20 don't think that accurately states</p> <p>21 the hypothesis.</p> <p>22 THE WITNESS: No. As you</p> <p>23 can see in this chart, low grade</p> <p>24 serous carcinoma, high grade</p>
<p style="text-align: right;">Page 419</p> <p>1 epithelium on ovarian and peritoneal</p> <p>2 surfaces resulting in a variety of low</p> <p>3 grade serous proliferations. If this</p> <p>4 hypothesis is confirmed it would indicate</p> <p>5 that all ovarian tumors, low and high</p> <p>6 grade, originate from tubal epithelium</p> <p>7 and involve the ovary secondarily."</p> <p>8 Did I read that correctly?</p> <p>9 A. That's what we wrote.</p> <p>10 Q. Okay. Now, Doctor, isn't it</p> <p>11 generally accepted today that ovarian</p> <p>12 serous tumors originate in the tubal</p> <p>13 epithelium?</p> <p>14 A. Okay. So we have two</p> <p>15 things. You're talking about low grade</p> <p>16 serous carcinoma right, or are you</p> <p>17 talking about high grade serous</p> <p>18 carcinoma?</p> <p>19 Q. You are talking about both</p> <p>20 in this paper, aren't you?</p> <p>21 A. Okay. So for the low grades</p> <p>22 it is a hypothesis, right? We</p> <p>23 hypothesize this and that.</p> <p>24 But for high grade serous</p>	<p style="text-align: right;">Page 421</p> <p>1 serous carcinoma, they are totally</p> <p>2 different.</p> <p>3 High grade serous carcinoma</p> <p>4 is a Type II. Low grade serous</p> <p>5 carcinoma is a Type I disease.</p> <p>6 Okay. So their origin is</p> <p>7 fallopian tube. By their</p> <p>8 pathogenesis, molecular genetic</p> <p>9 changes, they are all different.</p> <p>10 So you cannot lump them together</p> <p>11 for discussion.</p> <p>12 BY DR. RESTAINO:</p> <p>13 Q. Okay. If you go back to</p> <p>14 Page 2 --</p> <p>15 A. Which paper?</p> <p>16 Q. -- of your paper, please.</p> <p>17 The one we are talking about with</p> <p>18 Dr. Kurman, the papillary studies. If</p> <p>19 you go to Page 2, back to the top. The</p> <p>20 very last sentence above the line states,</p> <p>21 "If this hypothesis is confirmed, it can</p> <p>22 be concluded that low and high grade</p> <p>23 ovarian tumors develop from tubal</p> <p>24 epithelium and involve the ovary</p>

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<p style="text-align: right;">Page 422</p> <p>1 secondarily." 2 Did you conduct a follow-up 3 study to prove or disprove your 4 hypothesis? 5 MS. MILLER: Objection. 6 BY DR. RESTAINO: 7 Q. It's just yes or no. 8 A. So again you are confused 9 about low grade and high grade. They are 10 two different diseases. 11 Okay. For the low grade is 12 a hypothesis. And you know low grade 13 serous carcinoma is only 5 percent of 14 ovarian cancer. Really, really small 15 population. So I don't know whether low 16 grade serous carcinoma has been shown in 17 any epidemiology studies, any 18 epidemiology study break, high grade, low 19 grade, clear cell endometriosis, and et 20 cetera. Otherwise, I don't know what you 21 are talking about. 22 Q. Well, I'm talking about what 23 you wrote, sir. 24 A. Yes.</p>	<p style="text-align: right;">Page 424</p> <p>1 obviously an objectionable 2 question. 3 Objection. 4 BY DR. RESTAINO: 5 Q. Did the peer reviewers know 6 what you meant? 7 MS. MILLER: Objection. 8 THE WITNESS: Who are the 9 peer reviewers? 10 BY DR. RESTAINO: 11 Q. I'm sorry? 12 A. Who are the peer reviewers? 13 Q. Well, they are typically 14 anonymous, aren't they? 15 A. Yes. 16 Q. So I wouldn't know that. 17 But somebody peer reviewed this, don't 18 you agree? 19 MS. MILLER: Objection. 20 THE WITNESS: That's not 21 relevant to this question. 22 BY DR. RESTAINO: 23 Q. Okay. Doctor, in 2011, was 24 it biologically plausible that low and</p>
<p style="text-align: right;">Page 423</p> <p>1 Q. So I'm going to move to 2 strike your answer, because there's no 3 confusion on my part, because I can read 4 English. And what's stated here is if 5 this hypothesis is confirmed, then it can 6 be concluded that low and high grade 7 ovarian tumors developed from tubal 8 epithelium and involve the -- the ovary 9 secondarily. So I'm combining low grade 10 and high grade because that's what's 11 written here, correct, Doctor? 12 MR. LOCKE: Objection. 13 MS. SHARKO: Objection. 14 THE WITNESS: That's not how 15 we meant. 16 BY DR. RESTAINO: 17 Q. Oh, so is it your testimony 18 today that a future reader, when they 19 read this sentence, should call you up 20 and say, Dr. Shih, what did you mean by 21 this? 22 A. No. This the -- 23 MS. MILLER: Objection. 24 Give me time to object. That was</p>	<p style="text-align: right;">Page 425</p> <p>1 high grade ovarian tumors stimulated by 2 chronic inflammation develop in the tubal 3 epithelium, was it just biologically 4 plausible? 5 MS. MILLER: Objection. 6 Objection. Asked and answered. 7 THE WITNESS: No. 8 I answered your question. 9 BY DR. RESTAINO: 10 Q. Okay. When you submitted 11 the paper for publication, did any peer 12 reviewer come back and say, this is not 13 biologically plausible, we're not going 14 to publish this? 15 MS. MILLER: Objection. 16 THE WITNESS: Could you 17 repeat that question one more 18 time? 19 BY DR. RESTAINO: 20 Q. When you submitted the paper 21 for publication. 22 A. Yes. 23 Q. Did any peer reviewer come 24 back and say, this is not biologically</p>

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<p style="text-align: right;">Page 426</p> <p>1 plausible?</p> <p>2 A. In the peer review systems,</p> <p>3 my -- I serve editor-in-chief. This is</p> <p>4 not our focus. We want to publish</p> <p>5 hypothesis, review articles, epidemiology</p> <p>6 study, which don't have any biological</p> <p>7 plausibility, right?</p> <p>8 We publish all the data that</p> <p>9 is peer reviewed. So that's our job.</p> <p>10 It's not required, it's not required for</p> <p>11 any publication to need that biological</p> <p>12 plausibility.</p> <p>13 DR. RESTAINO: Move to</p> <p>14 strike as unresponsive.</p> <p>15 BY DR. RESTAINO:</p> <p>16 Q. Do you know what the peer</p> <p>17 reviewers --</p> <p>18 MS. MILLER: It was</p> <p>19 responsive.</p> <p>20 THE WITNESS: Why, why, why.</p> <p>21 BY DR. RESTAINO:</p> <p>22 Q. Do you know what the peer</p> <p>23 reviewers did in this case, did anyone</p> <p>24 say to you, this is not biologically</p>	<p style="text-align: right;">Page 428</p> <p>1 peer reviewers said, then you</p> <p>2 should tell him that.</p> <p>3 THE WITNESS: Oh, I cannot</p> <p>4 remember that.</p> <p>5 BY DR. RESTAINO:</p> <p>6 Q. Okay. And, Doctor --</p> <p>7 DR. RESTAINO: Thank you,</p> <p>8 Susan.</p> <p>9 BY DR. RESTAINO:</p> <p>10 Q. If you would turn now to</p> <p>11 your expert report, Page 9.</p> <p>12 A. Okay. I'm sorry. Which</p> <p>13 one, page?</p> <p>14 Q. Page 9 of your expert</p> <p>15 report, I think it is.</p> <p>16 The lack of sufficient</p> <p>17 evidence to support talc as a cause of</p> <p>18 ovarian cancer?</p> <p>19 A. You mean the C, right, under</p> <p>20 the Section C? We are looking at</p> <p>21 different pages.</p> <p>22 Q. Just give me a chance to get</p> <p>23 there. C, the lack of sufficient</p> <p>24 evidence to support talc as a cause of</p>
<p style="text-align: right;">Page 427</p> <p>1 plausible?</p> <p>2 MS. MILLER: Objection.</p> <p>3 THE WITNESS: I think I</p> <p>4 answered your question.</p> <p>5 BY DR. RESTAINO:</p> <p>6 Q. I'm -- I'm sorry, you</p> <p>7 didn't.</p> <p>8 Did you get something back</p> <p>9 from peer reviewers saying this is not</p> <p>10 biologically plausible, please provide</p> <p>11 more information or do this further</p> <p>12 study?</p> <p>13 MS. MILLER: Objection.</p> <p>14 THE WITNESS: I think I</p> <p>15 already answered your question.</p> <p>16 Biological plausibility is</p> <p>17 not required for any publications.</p> <p>18 MS. SHARKO: I can help you</p> <p>19 out. Dr. Shih --</p> <p>20 THE WITNESS: Yeah.</p> <p>21 MS. SHARKO: -- he's just</p> <p>22 asking you if any of the peer</p> <p>23 reviewers said that to you.</p> <p>24 So if you remember what the</p>	<p style="text-align: right;">Page 429</p> <p>1 ovarian cancer.</p> <p>2 Okay. In the middle</p> <p>3 paragraph, you have a section that starts</p> <p>4 "according to Merriam-Webster's</p> <p>5 dictionary."</p> <p>6 Do you see that, sir?</p> <p>7 A. Right.</p> <p>8 Q. Okay. Then the final two</p> <p>9 sentences to the -- that starts to the</p> <p>10 right of Martincorema 2017, you write,</p> <p>11 "Thus, in order to prove that any</p> <p>12 substance is carcinogenic it is not</p> <p>13 sufficient to demonstrate exposure. One</p> <p>14 must also demonstrate that the exposure</p> <p>15 can cause biological effects and</p> <p>16 tissue/cellular changes (like precursor</p> <p>17 lesions)."</p> <p>18 Did I read that correctly?</p> <p>19 A. Yes.</p> <p>20 Q. And is it still your opinion</p> <p>21 today that one must demonstrate the</p> <p>22 exposure causes biological effects and</p> <p>23 tissue/cellular changes?</p> <p>24 A. Cause biological effects,</p>

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<p style="text-align: right;">Page 430</p> <p>1 meaning biological plausibility to 2 support, to support this issue. 3 Q. I'm sorry, Doctor, you are 4 not saying biological plausibility here. 5 What you wrote here was very specific, 6 that "in order to prove that any 7 substance is carcinogenic, it is not 8 sufficient to demonstrate exposure, one 9 must also demonstrate the exposure can 10 cause biological effects and 11 tissue/cellular changes." 12 Is that still your opinion, 13 sir? 14 A. You need to see why I say 15 that. You cannot just quote -- quote one 16 sentence. 17 You see my previous 18 sentences. "Carcinogens cause cancer due 19 to their ability to damage DNA," blah, 20 blah, blah. 21 "Thus, in order to prove 22 that any substance is carcinogenic, it's 23 not sufficient to demonstrate exposure." 24 What I mean is the mere</p>	<p style="text-align: right;">Page 432</p> <p>1 evidence of -- of epidemiology exposure, 2 that there had to be scientific evidence 3 of mutagenic activity. Isn't that 4 correct? 5 MR. LOCKE: Objection to 6 form. 7 MS. MILLER: Objection. 8 MR. MIZGALA: Objection. 9 MS. MILLER: You got three 10 objections at the same time there. 11 Did you get them all? 12 THE WITNESS: Do you have 13 the reference or documents for 14 that? 15 BY DR. RESTAINO: 16 Q. Well, Doctor, I'll show you 17 what I've been marked as Shih-26. 18 (Document marked for 19 identification as Exhibit 20 Shih-26.) 21 BY DR. RESTAINO: 22 Q. It's a Saturday, 23 September 30, 1950, publication in the 24 British Medical Journal titled "Smoking</p>
<p style="text-align: right;">Page 431</p> <p>1 experience -- the appearance of 2 something, like talcum powder, I don't -- 3 I don't believe, I don't see any credible 4 evidence, ever in the fallopian tube, 5 beneath the epithelial cells, okay, if we 6 assume, but this is not possible, assume 7 it's there, it's not sufficient to 8 demonstrate that it is causal. You need 9 to provide biological evidence to 10 support, for example. 11 You need to show that talcum 12 powder existence, right, can support 13 there is a carcinogenic effect on the p53 14 signature. And a -- and a STIC and a 15 biological mechanism behind that. 16 There's many biological mechanisms. 17 That's why I say in -- in 18 reference to the previous sentence, 19 that's what I said. 20 Q. Doctor. 21 A. Right. 22 Q. That's the exact argument 23 tobacco industry made in the 1950s and 24 the 1960s that one cannot rely upon</p>	<p style="text-align: right;">Page 433</p> <p>1 and Carcinoma of the Lung," by Richard 2 Doll and Austin Bradford Hill. 3 A. Wow. 4 Q. Doctor, if you take a look 5 at it, the -- 6 A. Hold on a moment. I need to 7 see British Medical Journal. 1950. 8 Q. Now, sir, you see on the 9 right-hand column there's a heading 10 possible causes of the increase? 11 A. Could you hold a moment. I 12 need to see what is this article. 13 Q. What part -- what do you 14 need to look up for this article? 15 A. I want to know -- 16 Q. It's published in British 17 Medical Journal in 1950. It's written by 18 Sir Richard Doll and Sir Austin Bradford 19 Hill. What else do you need to see? 20 MS. MILLER: Objection. Is 21 that actually a question or are 22 you just being argumentative? If 23 you'd like him to answer, he can. 24 But I'm guessing you're just being</p>

<p style="text-align: right;">Page 434</p> <p>1 argumentative. Tempers are 2 flaring. The day's been long. 3 DR. RESTAINO: We've got 4 about nine minutes. 5 BY DR. RESTAINO: 6 Q. Doctor, look at, "Possible 7 causes of the increase. Two main causes 8 have from time to time been put forward." 9 A. Okay. I did not follow. I 10 just want to see any reference, okay. 11 That's a point. 12 Q. A pre-1950 reference is 13 going to help you? 14 A. No, no. Whether they cite 15 any references. That's what I'm going 16 to. Okay. 17 This one, two, three, four, 18 five, six, seven, eight references in 19 1947 and 1944, 1939. Okay. What's your 20 question? 21 Q. Possible causes of the 22 increase. 23 A. Wait, wait, wait a second. 24 Okay.</p>	<p style="text-align: right;">Page 436</p> <p>1 form," Counsel. You have really 2 crossed the line on this last one. 3 We've got seven minutes. Please, 4 or I'll call Judge Pisano. 5 THE WITNESS: So before I 6 can answer any question, I need 7 to -- so which -- which sentence 8 you are referring to? 9 BY DR. RESTAINO: 10 Q. Well, sir, I was referring 11 to the fact that the two -- of the two -- 12 A. Oh, the paragraph. 13 Q. -- causes listed there, one 14 of them is smoking of the -- smoking of 15 tobacco. 16 As a pathologist, in your 17 medical school education and in your 18 training as a pathologist, did you study 19 the association of smoking and lung 20 cancer? 21 MS. MILLER: So objection. 22 You said two main causes. And we 23 don't know of what. 24 DR. RESTAINO: I read them</p>
<p style="text-align: right;">Page 435</p> <p>1 Q. Front page, right column. 2 "Two main causes from time to time have 3 been put forward: One a general 4 atmospheric pollution from the exhaust 5 fumes of cars, from the surface dust of 6 tarred roads, and from gas-works, 7 industrial plants, and coal fires; and to 8 the smoking of tobacco." 9 Did I read that correctly? 10 MR. LOCKE: Objection. 11 MS. MILLER: I'm going to 12 raise several objections here. 13 The witness has never seen this. 14 This is outside his area of 15 expertise. You haven't given him 16 time to read it. And you've 17 plucked one sentence out of it in 18 order to make some point, unclear. 19 And I think that's grossly unfair. 20 THE WITNESS: This is 1950. 21 MS. MILLER: You can't ask a 22 scientist to comment on one 23 sentence -- 24 MS. PARFITT: "Object to</p>	<p style="text-align: right;">Page 437</p> <p>1 into the record, what they are. 2 MS. MILLER: Causes of what? 3 You just pulled out a sentence 4 that says "two main causes." Of 5 what? 6 DR. RESTAINO: How about the 7 title of the article? 8 MS. MILLER: Well, you 9 didn't even put that. I mean, he 10 hasn't had a chance to look at it. 11 THE WITNESS: So this is a 12 few sentences. Do you know how 13 many sentences here? 14 BY DR. RESTAINO: 15 Q. Yes. 16 A. How many sentences? 17 Q. I've read it. 18 A. Yeah, how many sentences? 19 Q. A lot. 20 A. Well, how many? 21 Q. Is it your opinion that -- 22 MS. MILLER: Not going to 23 argue. 24 BY DR. RESTAINO:</p>

<p style="text-align: right;">Page 438</p> <p>1 Q. -- that the association with 2 smoking and lung cancer established in 3 the 1950s and 1960s by case-control 4 epidemiological studies depended upon the 5 molecular evidence that you put into your 6 record that must be present for there to 7 be an association? 8 MS. MILLER: Objection. 9 MR. LOCKE: Objection to 10 form and beyond the scope. 11 MS. MILLER: Thank you. 12 Because I've been chided for 13 apparently objecting improperly. 14 MS. PARFITT: Counsel, I'm 15 just following the CMO. 16 MS. MILLER: Did you guys 17 follow the CMO when you were 18 defending depositions? 19 BY DR. RESTAINO: 20 Q. Can you answer the question, 21 Doctor? 22 A. I am a gynecology 23 pathologist. My field of research is 24 vulva, vagina, cervix, uterus, right</p>	<p style="text-align: right;">Page 440</p> <p>1 and ask me one by one? Thank you very 2 much. 3 Q. Doctor -- 4 A. Yes. 5 Q. -- carcinogen causes cancer 6 due to their ability to damage the genome 7 and induce a cancer driver but not 8 passenger mutations that promote cancer 9 development; is that correct? 10 A. I need to see that, please. 11 Q. Just read from your paper. 12 I'm reading what you wrote. 13 A. Yeah, I need to -- do you 14 remember when I said that, in what 15 context? What kind of question you ask? 16 Q. You need to have context for 17 knowing -- for answering whether or not 18 the word ovary is in that paragraph? 19 MS. MILLER: Objection. 20 THE WITNESS: Ovary in the 21 paragraph. 22 MS. MILLER: Please, Doctor, 23 let me do my job. 24 THE WITNESS: Okay. Okay.</p>
<p style="text-align: right;">Page 439</p> <p>1 fallopian tube, left fallopian tube, 2 right ovary, and the left ovary. 3 Q. Okay. And, Doctor, in that 4 paragraph that you wrote at the bottom of 5 the page where you start with, "According 6 to Merriam-Webster's dictionary," and you 7 describe a carcinogen as a substance that 8 causes cancer, every one of those 9 anatomic parts that you just said are not 10 in this paragraph, correct? 11 MS. MILLER: Objection. 12 BY DR. RESTAINO: 13 Q. This paragraph talks about 14 cancer in general, does it not? 15 MS. MILLER: Objection. 16 MR. LOCKE: Objection. 17 MS. MILLER: There's two 18 questions there. 19 THE WITNESS: You speak too 20 fast. This embedded different 21 questions. 22 BY DR. RESTAINO: 23 Q. Okay. 24 A. Could you dissect this out</p>	<p style="text-align: right;">Page 441</p> <p>1 What do you mean ovary in 2 that paragraph? I'm confused. 3 BY DR. RESTAINO: 4 Q. Doctor, this paragraph 5 describes what carcinogens are in a 6 general sense, not limited to the 7 genitourinary tracts of a woman, correct? 8 A. You mean this paragraph 9 in -- in "Smoking and Carcinoma of the 10 Lung"? 11 Q. No, Doctor. 12 A. Which -- which paragraph are 13 you referring to? 14 Q. The paragraph we're reading 15 from Page 9 of your expert report -- 16 A. Page 9, okay. 17 Q. "Lack of sufficient evidence 18 to support talc as a cause of ovarian 19 cancer. 20 A. Where is that now? 21 Q. On Page 9, C. 22 A. Okay. C, yes. 23 Q. You asked me about letter C. 24 Letter C, "The lack of sufficient</p>

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<p style="text-align: right;">Page 442</p> <p>1 evidence to support talc as a cause of 2 ovarian cancer." 3 In the paragraph, "according 4 to Merriam-Webster's dictionary," you do 5 not describe the ovaries, nor the 6 genitourinary tract, but rather you 7 discuss carcinogens and cancer in a 8 general sense, do you not? 9 MS. MILLER: Objection. 10 THE WITNESS: Okay. So your 11 question is you talk about the 12 definition of the carcinogen and I 13 did not have over here. And you 14 said this is the general 15 description. 16 BY DR. RESTAINO: 17 Q. Correct? Correct? 18 A. That's from the definition 19 of the dictionary. 20 Q. So is your opinion outside 21 the genitourinary tract, but as cancer in 22 general, that one must also demonstrate 23 exposure can cause biological effects and 24 tissue/cellular changes like precursor</p>	<p style="text-align: right;">Page 444</p> <p>1 approximately 6:00 p.m.) 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24</p>
<p style="text-align: right;">Page 443</p> <p>1 lesions before you can make a causal 2 connection between an environmental 3 carcinogen and cancer? 4 A. No -- 5 MR. LOCKE: Objection. 6 MR. MIZGALA: Objection. 7 BY DR. RESTAINO: 8 Q. Okay. 9 A. Is not must. Is has the 10 biological plausibility to support. 11 That's what I mean. 12 DR. RESTAINO: Okay. I 13 think we're done. 14 MS. SHARKO: Thank you very 15 much. 16 DR. RESTAINO: No further 17 questions. 18 THE VIDEOGRAPHER: The time 19 is 6:00 p.m. March 26, 2019. 20 Going off the record. 21 This ends the videotaped 22 deposition. 23 (Excused.) 24 (Deposition concluded at</p>	<p style="text-align: right;">Page 445</p> <p>1 2 CERTIFICATE 3 4 5 I HEREBY CERTIFY that the 6 witness was duly sworn by me and that the 7 deposition is a true record of the 8 testimony given by the witness. 9 10 It was requested before 11 completion of the deposition that the 12 witness, IE-MING SHIH, M.D., Ph.D., have 13 the opportunity to read and sign the 14 deposition transcript. 15 16 MICHELLE L. GRAY, 17 A Registered Professional 18 Reporter, Certified Shorthand 19 Reporter, Certified Realtime 20 Reporter and Notary Public 21 Dated: March 27, 2019 22 23 (The foregoing certification 24 of this transcript does not apply to any reproduction of the same by any means, unless under the direct control and/or supervision of the certifying reporter.)</p>

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<p>1 INSTRUCTIONS TO WITNESS</p> <p>2</p> <p>3 Please read your deposition</p> <p>4 over carefully and make any necessary</p> <p>5 corrections. You should state the reason</p> <p>6 in the appropriate space on the errata</p> <p>7 sheet for any corrections that are made.</p> <p>8 After doing so, please sign</p> <p>9 the errata sheet and date it.</p> <p>10 You are signing same subject</p> <p>11 to the changes you have noted on the</p> <p>12 errata sheet, which will be attached to</p> <p>13 your deposition.</p> <p>14 It is imperative that you</p> <p>15 return the original errata sheet to the</p> <p>16 deposing attorney within thirty (30) days</p> <p>17 of receipt of the deposition transcript</p> <p>18 by you. If you fail to do so, the</p> <p>19 deposition transcript may be deemed to be</p> <p>20 accurate and may be used in court.</p> <p>21</p> <p>22</p> <p>23</p> <p>24</p>	<p>1</p> <p>2 ACKNOWLEDGMENT OF DEPONENT</p> <p>3</p> <p>4 I, _____, do</p> <p>5 hereby certify that I have read the</p> <p>6 foregoing pages, 1 - 449, and that the</p> <p>7 same is a correct transcription of the</p> <p>8 answers given by me to the questions</p> <p>9 therein propounded, except for the</p> <p>10 corrections or changes in form or</p> <p>11 substance, if any, noted in the attached</p> <p>12 Errata Sheet.</p> <p>13</p> <p>14</p> <p>15 _____</p> <p>16 IE-MING SHIH, M.D., Ph.D. DATE</p> <p>17</p> <p>18</p> <p>19 Subscribed and sworn</p> <p>20 to before me this</p> <p>21 _____ day of _____, 20 ____.</p> <p>22 My commission expires: _____</p> <p>23 _____</p> <p>24 Notary Public</p>
Page 447	Page 449
<p>1 - - - - -</p> <p>2 E R R A T A</p> <p>3 - - - - -</p> <p>4 PAGE LINE CHANGE</p> <p>5 _____</p> <p>6 REASON: _____</p> <p>7 _____</p> <p>8 REASON: _____</p> <p>9 _____</p> <p>10 REASON: _____</p> <p>11 _____</p> <p>12 REASON: _____</p> <p>13 _____</p> <p>14 REASON: _____</p> <p>15 _____</p> <p>16 REASON: _____</p> <p>17 _____</p> <p>18 REASON: _____</p> <p>19 _____</p> <p>20 REASON: _____</p> <p>21 _____</p> <p>22 REASON: _____</p> <p>23 _____</p> <p>24 REASON: _____</p>	<p>1 LAWYER'S NOTES</p> <p>2 PAGE LINE</p> <p>3 _____</p> <p>4 _____</p> <p>5 _____</p> <p>6 _____</p> <p>7 _____</p> <p>8 _____</p> <p>9 _____</p> <p>10 _____</p> <p>11 _____</p> <p>12 _____</p> <p>13 _____</p> <p>14 _____</p> <p>15 _____</p> <p>16 _____</p> <p>17 _____</p> <p>18 _____</p> <p>19 _____</p> <p>20 _____</p> <p>21 _____</p> <p>22 _____</p> <p>23 _____</p> <p>24 _____</p>

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Exhibit C

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Page 1

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE: JOHNSON &)
JOHNSON TALCUM POWDER)
PRODUCTS MARKETING)
SALES PRACTICES AND) MDL 16-2738
PRODUCT LIABILITY) (FLW)(LHG)
LITIGATION)
_____)
THIS DOCUMENT)
PERTAINS TO ALL CASES)

MONDAY, APRIL 8, 2019

CONFIDENTIAL - PURSUANT TO PROTECTIVE ORDER

- - -

Videotaped deposition of Jeffrey A.
Boyd, Ph.D., held at the offices of Shook,
Hardy & Bacon LLP, 201 South Biscayne
Boulevard, Suite 3200, Miami, Florida,
commencing at 9:03 a.m., on the above date,
before Carrie A. Campbell, Registered
Diplomate Reporter and Certified Realtime
Reporter.

- - -

GOLKOW LITIGATION SERVICES
877.370.3377 ph | 917.591.5672 fax
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Jeffrey A. Boyd, Ph.D.

Page 2	Page 4
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Page 3	Page 5
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<p style="text-align: right;">Page 6</p> <p>1 Boyd 19 GYN-18-1020: Final Decision 274 Letter to Dr. Saed</p> <p>2 Boyd 20 Mg3Si2O5(OH)4 283</p> <p>3 Boyd 21 "Identifying postmenopausal 299 4 women at elevated risk for epithelial ovarian cancer," 5 Urban, et al.</p> <p>6 Boyd 22 "Role of CA125 in predicting 303 7 ovarian cancer survival -a review of the epidemiological 8 literature," Gupta, et al.</p> <p>9 Boyd 23 "Tumor-associated 307 10 autoantibodies as early detection markers for ovarian 11 cancer? A prospective evaluation," Kaaks, et al.</p> <p>12 Boyd 24 "Ovarian cancer screening and 310 13 mortality in the UK Collaborative Trial of Ovarian Cancer Screening (UKTOCS): A 14 randomised controlled trial," Jacobs, et al.</p> <p>15 Boyd 25 "Early Detection of Ovarian 314 Cancer," Elias, et al.</p> <p>16 Boyd 26 "The MPO-463 G> A polymorphism 326 17 and cancer risk: A meta-analysis based on 43 18 case-control studies," Chu, et al.</p> <p>19 Boyd 27 "Opportunities and challenges 344 20 in ovarian cancer research, a perspective from the 11th 21 Ovarian cancer action-HHMT Forum, Lake Como, March 2007," 22 Gynecologic Oncology 23 24 25</p>	<p style="text-align: right;">Page 8</p> <p>1 DIRECT EXAMINATION</p> <p>2 QUESTIONS BY MR. RESTAINO:</p> <p>3 Q. Good morning, Dr. Boyd.</p> <p>4 A. Good morning.</p> <p>5 Q. Before the deposition started,</p> <p>6 I introduced myself, but for the record, my</p> <p>7 name is John Restaino. And stating the</p> <p>8 obvious, I'm representing the plaintiffs in</p> <p>9 this litigation.</p> <p>10 It's my understanding that</p> <p>11 you've had your deposition taken at least</p> <p>12 twice before; is that correct?</p> <p>13 A. Yes.</p> <p>14 Q. So you're vaguely aware of the</p> <p>15 rules that we'll be operating under today; is</p> <p>16 that correct?</p> <p>17 A. Yes.</p> <p>18 Q. Okay. In essence, this is not</p> <p>19 a memory test, so if you need to refer to a</p> <p>20 document, it's open book.</p> <p>21 It's not a physical test, so</p> <p>22 we'll try to take a take break about every</p> <p>23 hour, hour and 15 minutes or so. However, in</p> <p>24 between breaks, if you need to take a break</p> <p>25 for whatever reason, assuming there isn't a</p>
<p style="text-align: right;">Page 7</p> <p>1 VIDEOGRAPHER: We are on the</p> <p>2 record. My name is Devyn Mulholland.</p> <p>3 I'm a videographer with Golkow</p> <p>4 Litigation Services.</p> <p>5 Today's date is April 8, 2019.</p> <p>6 The time is 9:03 a.m.</p> <p>7 This video deposition is being</p> <p>8 held in Miami, Florida, in the matter</p> <p>9 of talcum powder litigation.</p> <p>10 The deponent is Jeff Boyd,</p> <p>11 Ph.D.</p> <p>12 Counsel will be noted on the</p> <p>13 stenographic record.</p> <p>14 The court reporter is Carrie</p> <p>15 Campbell, who will now swear in the</p> <p>16 witness.</p> <p>17</p> <p>18 JEFFREY A. BOYD, Ph.D.,</p> <p>19 of lawful age, having been first duly sworn</p> <p>20 to tell the truth, the whole truth and</p> <p>21 nothing but the truth, deposes and says on</p> <p>22 behalf of the Plaintiffs, as follows:</p> <p>23</p> <p>24</p> <p>25</p>	<p style="text-align: right;">Page 9</p> <p>1 question pending, just let us know and we'll</p> <p>2 accommodate that.</p> <p>3 A. Thank you.</p> <p>4 Q. Understand?</p> <p>5 There are times when, based</p> <p>6 upon my question -- this is extremely rare --</p> <p>7 but Jessica may object to my questions,</p> <p>8 because usually my questions are perfect.</p> <p>9 That's -- unless counsel instructs you not to</p> <p>10 answer, it's the lawyers, in essence,</p> <p>11 protecting the record for each perspective.</p> <p>12 I don't get to say "objective,"</p> <p>13 {sic} but if I ask you a particular question</p> <p>14 and then I don't think you answered my</p> <p>15 question, I may say "move to strike as</p> <p>16 unresponsive." I'm not being rude. Once</p> <p>17 again, we're making the record.</p> <p>18 Do you understand?</p> <p>19 A. Yes.</p> <p>20 Q. Okay. And with that, so far</p> <p>21 we're off to a good start. There's the</p> <p>22 lovely lady to your right, my left, and she's</p> <p>23 going to try to take down everything that we</p> <p>24 each say.</p> <p>25 If two individuals are talking</p>

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<p style="text-align: right;">Page 10</p> <p>1 at a bar, having a drink, it's very common to</p> <p>2 step on each other's lines. Not being rude,</p> <p>3 just normal discourse, but it'll make her</p> <p>4 life a little tougher. So if you try to</p> <p>5 listen for the question mark at the end of my</p> <p>6 questions, and I'll try to listen to the</p> <p>7 period. And if I step on your answer, it's</p> <p>8 not intentional and I'll apologize, but let's</p> <p>9 try to keep it clean for her.</p> <p>10 Make sense?</p> <p>11 A. Fair enough.</p> <p>12 Q. If I ask you a question and you</p> <p>13 answer it, we will assume you understood the</p> <p>14 question. So therefore, if you don't</p> <p>15 understand the question, please let me know,</p> <p>16 and I'll try to rephrase it in a more</p> <p>17 understandable manner.</p> <p>18 Understood?</p> <p>19 A. Yes.</p> <p>20 Q. And no one in the room wants</p> <p>21 you to guess today, though there may be times</p> <p>22 when an estimate is in order. And I'm not</p> <p>23 going to insult your intelligence as to the</p> <p>24 difference between a guess and an estimate.</p> <p>25 I'm sure you know that.</p>	<p style="text-align: right;">Page 12</p> <p>1 to say, he doesn't have those</p> <p>2 responses.</p> <p>3 MR. RESTAINO: Yeah.</p> <p>4 QUESTIONS BY MR. RESTAINO:</p> <p>5 Q. And if you notice again, on the</p> <p>6 third to last page there's some other</p> <p>7 documents that are attached to this which</p> <p>8 I've marked -- this is the Johnson & Johnson</p> <p>9 response to the notice, production-marked as</p> <p>10 number 2, and there's a supplemental</p> <p>11 materials considered, and the page after that</p> <p>12 a correspondence from you to a Jessica</p> <p>13 Miller, and then on the last page an invoice</p> <p>14 with a redaction in the center.</p> <p>15 Do you see that, sir?</p> <p>16 A. Yes.</p> <p>17 Q. And have you seen this before?</p> <p>18 A. Yes.</p> <p>19 Q. Okay. When did you see this,</p> <p>20 other than this morning?</p> <p>21 A. Well, if we go back to the</p> <p>22 third from last page, we -- I looked at this</p> <p>23 briefly yesterday afternoon.</p> <p>24 Q. Okay.</p> <p>25 A. And, of course, the invoice and</p>
<p style="text-align: right;">Page 11</p> <p>1 So in essence, no guessing</p> <p>2 today. Just if you're not sure, just let us</p> <p>3 know or give us your best estimate.</p> <p>4 Do you understand that?</p> <p>5 A. Yes.</p> <p>6 Q. Before the deposition started,</p> <p>7 I premarked a couple of exhibits to save a</p> <p>8 little bit of time. And the first one is the</p> <p>9 notice of your deposition. And I'm going to</p> <p>10 hand you this now.</p> <p>11 (Boyd Exhibits 1 and 2 marked</p> <p>12 for identification.)</p> <p>13 QUESTIONS BY MR. RESTAINO:</p> <p>14 Q. And, Dr. Boyd, have you seen</p> <p>15 this before?</p> <p>16 A. I don't remember seeing it, no.</p> <p>17 Q. Okay. In response to it, and</p> <p>18 it might be a little easier to go along, the</p> <p>19 attorneys for Johnson & Johnson has filed a</p> <p>20 response to that. And glance through it.</p> <p>21 Not only are there responses, but if you see</p> <p>22 on the third to last page there's</p> <p>23 supplemental materials considered on this</p> <p>24 form here. I'm going to hand them -- sorry.</p> <p>25 MS. MILLER: Yeah, I was going</p>	<p style="text-align: right;">Page 13</p> <p>1 the accompanying documentation underlying the</p> <p>2 invoice, I obviously saw it on or about</p> <p>3 February 25th.</p> <p>4 Q. Okay. And you said that if we</p> <p>5 go back to the third from last page, "I</p> <p>6 looked at this briefly yesterday afternoon."</p> <p>7 And this is a supplemental materials</p> <p>8 considered, correct? On the third to last</p> <p>9 page?</p> <p>10 A. Yes, you've read it correctly.</p> <p>11 Q. Did you type this up?</p> <p>12 A. No.</p> <p>13 Q. Do you know who typed it up?</p> <p>14 A. No.</p> <p>15 Q. Have you, in fact, reviewed the</p> <p>16 documents that are listed on this page?</p> <p>17 A. At least in very cursory</p> <p>18 fashion, yes.</p> <p>19 Q. Each and every one of them?</p> <p>20 A. Yes.</p> <p>21 (Boyd Exhibit 3 marked for</p> <p>22 identification.)</p> <p>23 QUESTIONS BY MR. RESTAINO:</p> <p>24 Q. I'm also going to mark -- or I</p> <p>25 have marked as number 3 the testifying</p>

4 (Pages 10 to 13)

Jeffrey A. Boyd, Ph.D.

<p style="text-align: right;">Page 14</p> <p>1 history for Jeff Boyd, Ph.D. 2 Have you seen this before? 3 A. Yes. 4 Q. And is that accurate? 5 MS. MILLER: So I would like to 6 just say something because obviously 7 my paralegal typed this up, and she 8 should have put within the last -- she 9 should have specified within how many 10 years. I mean, this was done pursuant 11 to the Federal Rules. 12 I just didn't want it to 13 suggest that it's the full testifying 14 history. 15 MR. RESTAINO: Let the record 16 denote that, and I assumed that. 17 MS. MILLER: Okay. 18 MR. RESTAINO: Thank you, 19 Jessica. 20 QUESTIONS BY MR. RESTAINO: 21 Q. Is that accurate for your 22 deposition in the last four years? 23 A. My testifying history? 24 Q. Yes. 25 A. Yes.</p>	<p style="text-align: right;">Page 16</p> <p>1 had one as well and so sought to prevent the 2 development of the aforementioned bone marrow 3 transplant unit at the Miami Cancer Institute 4 with some type of -- some type of legal suit, 5 for lack of a better term. 6 Q. Okay. 7 A. Which landed us in what I 8 recall as an administrative-type litigation 9 as opposed to, for example, a criminal or -- 10 Q. Understood. 11 A. -- some other type. 12 And we were deposed and 13 appeared before an administrative court judge 14 in Tallahassee. 15 Q. When you're saying "we," were 16 you a witness, a party or an expert or 17 something else in that litigation? 18 A. I would have to say this being 19 a very new kind of litigation to me, I would 20 have classified myself -- I seem tongue -- 21 tongue-tied this morning, I'm sorry -- as a 22 witness. 23 Q. Okay. Essentially the same 24 thing for the second one, the -- again, I see 25 a State of Florida Division of Administrative</p>
<p style="text-align: right;">Page 15</p> <p>1 Q. The first one, University of 2 Miami versus Agency for Health Care 3 Administration and Baptist Hospital of Miami, 4 Inc., what were the underlying facts of that 5 case, if you recall? 6 A. The Miami Cancer Institute and 7 Baptist Hospital of Miami, Inc., were filing 8 a certificate of need for a bone marrow 9 transplant unit at the Miami Cancer Institute 10 through the Florida Department of Health or 11 the Agency for Health Care Administration. I 12 think they're closely linked, to the best of 13 my knowledge. And the state, the agency, the 14 Florida Agency for Health Care 15 Administration, the Florida Department of 16 Health, to the best of my knowledge, in a CON 17 case, granted or allowed the certificate of 18 need, thus allowing us to establish a bone 19 marrow transplant unit at the Miami Cancer 20 Institute. 21 And to the best of my 22 knowledge, the University of Miami, 23 specifically the Sylvester Cancer Center, 24 took issue with Miami Cancer Institute having 25 a bone marrow transplant unit because they</p>	<p style="text-align: right;">Page 17</p> <p>1 hearings, so similar type of hearing? 2 A. It was basically a ditto. 3 Q. Okay. 4 A. We lost, "we" being Miami 5 Cancer Institute, Baptist Hospital, the first 6 case. 7 Lather, rinse, repeat. We 8 filed another CON that was approved by the 9 State. University of Miami sued. Went back 10 to the administrative court with a different 11 judge, and he ruled in our favor. 12 Q. And you had a similar -- 13 A. We now have a bone marrow 14 transplant unit at the Miami Cancer 15 Institute. 16 I'm sorry for interrupting you. 17 Q. And I'm sorry for interrupting 18 you. 19 And essentially the same role 20 in the second proceeding, as a witness? 21 A. Yes. 22 Q. Okay. Now, my understanding is 23 you're charging \$600 an hour for the document 24 type of review in this litigation? 25 A. Yes.</p>

5 (Pages 14 to 17)

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<p style="text-align: right;">Page 18</p> <p>1 Q. And you're charging \$1,200 per 2 hour for deposition and other testimony? 3 A. Yes. 4 Q. When is the last time, if ever, 5 you've been an expert witness in a 6 litigation? 7 A. Other than for my employer? 8 Q. Yes. 9 A. And here we're going to get 10 into the realm of an estimate, I guess. It 11 would have been the late '90s, early 2000s. 12 Q. Okay. Were you charging \$1,200 13 an hour for deposition testimony then? 14 A. My memory is that I was 15 charging 400, 800. 16 Q. Okay. When did you start 17 charging \$1,200 an hour? 18 A. Well, at the beginning of this 19 proceeding. 20 Q. Okay. Today we're going to be 21 here, and as you'll probably hear several 22 times, attorneys from both sides will be 23 asking the videographer how much time is on 24 the tape, because by the Federal Rules we get 25 seven hours of questioning. So you will be</p>	<p style="text-align: right;">Page 20</p> <p>1 correct. 2 Q. Another one of those estimate 3 questions. Can you estimate for us the 4 number of hours you have now between February 5 21st and April 7th? 6 MS. MILLER: Remember not to 7 guess. 8 THE WITNESS: I think a 9 reasonable estimate would be somewhere 10 between 70 and 100 hours. 11 QUESTIONS BY MR. RESTAINO: 12 Q. Okay. And because that's for 13 document review, that would be at the 14 \$600-an-hour rate? 15 A. Yes. 16 (Boyd Exhibit 4 marked for 17 identification.) 18 QUESTIONS BY MR. RESTAINO: 19 Q. Okay. I've now marked as 20 Plaintiff 4 the version of your CV that we've 21 received. 22 To the best of your knowledge, 23 is that a current CV? 24 A. As of February the 4th, 2019, 25 it would certainly have been an accurate,</p>
<p style="text-align: right;">Page 19</p> <p>1 charging Johnson & Johnson the \$1,200 for 2 those seven hours? 3 MS. MILLER: Objection. 4 QUESTIONS BY MR. RESTAINO: 5 Q. \$1,200 an hour for those seven 6 hours? 7 MS. MILLER: Objection. 8 THE WITNESS: Again, I'm sorry, 9 I don't do this a lot. My 10 understanding is that I send an 11 invoice to Ms. Miller, and the one 12 time I've done it, I received a check 13 from Skadden. 14 I honestly don't know how money 15 changes hands in these circumstances, 16 but I will be submitting -- I'm sorry, 17 I will be submitting an invoice to 18 Ms. Miller. 19 QUESTIONS BY MR. RESTAINO: 20 Q. Okay. And the last page of 21 Exhibit 2, I believe, is the invoice between 22 December 18th and February 21st; is that 23 correct? 24 A. It is an invoice for the period 25 between December 18th and February 21st,</p>	<p style="text-align: right;">Page 21</p> <p>1 up-to-date CV. 2 Q. And I will represent to you 3 that I have not added nor taken anything out 4 of your CV. 5 A. Thank you. 6 Q. And I'm sorry, Doctor, you said 7 that it was current as of February 4th. 8 As you sit here today, is there 9 anything that's been -- that needs to be 10 added or any publication that's coming out 11 that's specifically germane to talc, 12 inflammation, ovarian cancer, the reason why 13 we're here? 14 Anything new that will be 15 coming out? 16 MS. MILLER: Objection. 17 THE WITNESS: No. 18 QUESTIONS BY MR. RESTAINO: 19 Q. Okay. You understood that 20 question? 21 Because that wasn't a great 22 question. 23 MS. MILLER: That's why I 24 objected. 25 MR. RESTAINO: Yeah. Let the</p>

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<p style="text-align: right;">Page 22</p> <p>1 record denote that's the first time.</p> <p>2 MS. MILLER: Are you keeping a</p> <p>3 count today?</p> <p>4 THE WITNESS: I understood the</p> <p>5 question.</p> <p>6 QUESTIONS BY MR. RESTAINO:</p> <p>7 Q. Okay.</p> <p>8 A. And I stand behind my answer.</p> <p>9 Q. Now, prior to the deposition</p> <p>10 started, there was a little bit of a</p> <p>11 communication or discussion between yourself</p> <p>12 and Dr. Jennifer Emmel sitting to my right.</p> <p>13 Do you recall meeting with</p> <p>14 Dr. Emmel before?</p> <p>15 A. No.</p> <p>16 Q. Do you have -- if you met with</p> <p>17 an attorney in, say, March of 2017, would you</p> <p>18 keep records of any notes that you took?</p> <p>19 A. Well, that's very hard to say</p> <p>20 because I don't remember meeting with an</p> <p>21 attorney in March of 2017.</p> <p>22 Q. Okay. Fair enough. If you</p> <p>23 don't remember, you don't remember.</p> <p>24 MS. MILLER: We seem to be</p> <p>25 having this issue arise multiple</p>	<p style="text-align: right;">Page 24</p> <p>1 Q. In the request to produce, if</p> <p>2 you look at number 3, Request to Produce</p> <p>3 Number 3 --</p> <p>4 A. Number 3 what?</p> <p>5 Q. On the request to produce,</p> <p>6 which is on Exhibit Number 2. And so you</p> <p>7 have to turn to --</p> <p>8 A. What is number 3 in Exhibit</p> <p>9 Number 2, please?</p> <p>10 MS. MILLER: Wait. So here you</p> <p>11 go, Doctor. There's stickies at the</p> <p>12 bottom of the page. That's Exhibit 2.</p> <p>13 THE WITNESS: Yes.</p> <p>14 MS. MILLER: And he wants you</p> <p>15 to go to request -- this is just all</p> <p>16 like legal garble. It's mumbo jumbo.</p> <p>17 And he wants you to --</p> <p>18 THE WITNESS: I'm just not sure</p> <p>19 what number 3 means. I'm sorry.</p> <p>20 MS. MILLER: Request Number 3.</p> <p>21 THE WITNESS: Okay. So I'm on</p> <p>22 the page.</p> <p>23 QUESTIONS BY MR. RESTAINO:</p> <p>24 Q. Okay. And it asks for your</p> <p>25 complete file or files related to the work</p>
<p style="text-align: right;">Page 23</p> <p>1 times.</p> <p>2 QUESTIONS BY MR. RESTAINO:</p> <p>3 Q. If we look at the -- your</p> <p>4 response, so Exhibit 2, I believe, you see</p> <p>5 that there's specific requests. And I'm not</p> <p>6 going to spend a lot of time going through</p> <p>7 it, but if you start off with Request</p> <p>8 Number 3, your complete file or files.</p> <p>9 Do you have a file in this</p> <p>10 litigation, and if so, have you previously</p> <p>11 produced it to your counsel?</p> <p>12 MS. MILLER: Wait a minute.</p> <p>13 We're not his counsel. We're J&J's</p> <p>14 counsel. So...</p> <p>15 QUESTIONS BY MR. RESTAINO:</p> <p>16 Q. Let me rephrase that by saying</p> <p>17 have you previously produced it to counsel</p> <p>18 for J&J, representing J&J here today?</p> <p>19 A. I'm sorry, but that was a very</p> <p>20 long question, statement.</p> <p>21 Q. Yeah, let me just reask it.</p> <p>22 A. Can we just start over, please?</p> <p>23 Q. Of course.</p> <p>24 A. Perhaps parse the -- I'm sorry,</p> <p>25 perhaps parse the questions?</p>	<p style="text-align: right;">Page 25</p> <p>1 done.</p> <p>2 Have you previously produced to</p> <p>3 counsel for Johnson & Johnson your file or</p> <p>4 files in this regard?</p> <p>5 A. Again, could you repeat the</p> <p>6 question, please?</p> <p>7 Q. Request Number 3 asks for a</p> <p>8 copy of your complete file or files related</p> <p>9 to work on -- concerning talcum powder</p> <p>10 litigation, talcum powder products or talc in</p> <p>11 general.</p> <p>12 Have you produced any such</p> <p>13 files?</p> <p>14 A. No.</p> <p>15 Q. Are there files that you have</p> <p>16 back at your office?</p> <p>17 A. Pertaining to Request Number 3?</p> <p>18 Q. Yes.</p> <p>19 A. No.</p> <p>20 Q. Are there files anywhere else?</p> <p>21 A. No.</p> <p>22 Q. The reason I'm confused is</p> <p>23 because I asked you if you've produced a copy</p> <p>24 of your complete file or files to counsel for</p> <p>25 Johnson & Johnson, and your answer was no.</p>

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<p style="text-align: right;">Page 26</p> <p>1 A. Let's back up a little bit, 2 please. 3 First of all, I have two 4 offices, I have a study at home, and I have 5 no files at either work-related office or in 6 my study at home related to this matter. 7 Q. Okay. 8 MS. MILLER: I think he was 9 saying he didn't produce anything 10 because he didn't have anything. 11 I assume that's what you were 12 saying. That's how I understood it. 13 THE WITNESS: I don't have 14 anything. Certainly I keep records of 15 the time spent researching in order to 16 provide an accurate invoice, but other 17 than that, I have no files. 18 QUESTIONS BY MR. RESTAINO: 19 Q. Okay. Fair enough. 20 If you go down now to Request 21 Number 7, and there it's asking for articles, 22 papers and/or scientific, technical 23 publications written, prepared and/or 24 presented by you or in which you participated 25 in writing, preparing or presenting that</p>	<p style="text-align: right;">Page 28</p> <p>1 A. Yes. 2 Q. Okay. And I can skip a few 3 more. 4 If you skip down to Request 5 Number 15, and I'll wait for you to get 6 there. "All documents related to 7 communications with employees, 8 representatives, editors, or reviewers of any 9 scientific or medical journal which discuss 10 talcum powder products, talc and/or talcum 11 powder." 12 Are there any such documents? 13 A. No. 14 Q. And number 17 is "any slide 15 decks" -- 16 "Slide decks," old term. 17 A. It's a colloquialism. 18 Q. Back in the day. 19 -- "outlines, presentations or 20 other materials you've created or utilized in 21 connection with any presentation on talcum 22 powder, talc, and/or talcum powder products." 23 Do any of those exist? 24 A. No. 25 Q. And can we just have a general</p>
<p style="text-align: right;">Page 27</p> <p>1 relate or concern talcum powder products, 2 talc and talcum powder. 3 And if there are any such 4 publications, articles, papers, have you 5 previously produced them to counsel for 6 Johnson & Johnson? 7 MS. MILLER: Objection. 8 There's a couple of questions embedded 9 in there. It might be better to first 10 ask him if he has them and then if 11 he's produced them, because I think 12 that created a little bit of confusion 13 on the last round of questions. 14 QUESTIONS BY MR. RESTAINO: 15 Q. Okay. Doctor, as per Request 16 Number 7, do you have any "articles, papers, 17 scientific and/or technical publications 18 written, prepared and/or presented by you or 19 in which you participated in writing, 20 preparing or presenting that relate or 21 concern talcum powder products, talc and/or 22 talcum powder"? 23 A. My expert report. 24 Q. Okay. And that would be the 25 totality of it?</p>	<p style="text-align: right;">Page 29</p> <p>1 understanding sitting here in 2019 that slide 2 decks would also consider like PowerPoint 3 presentations? 4 A. That's how I refer to my 5 PowerPoint presentations, yes. 6 Q. You give presentations at 7 medical and/or scientific society meetings or 8 programs? 9 A. Yes. 10 Q. Do you show up with that little 11 round carousel of slides anymore, or do you 12 show up with a PowerPoint? 13 A. A, not for a long time; and B, 14 yes. 15 Q. Okay. If we go to the back of 16 your Exhibit 2 and point out the supplemental 17 materials that were considered, that I 18 believe you testified to that you saw 19 yesterday. 20 A. Yes. 21 Q. Okay. The first one is 22 deposition of Benjamin Neel. 23 Do you know who Dr. Neel is? 24 A. Yes. 25 Q. And that's N-e-e-l.</p>

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<p style="text-align: right;">Page 30</p> <p>1 Prior to this litigation, did 2 you know Dr. Benjamin Neel? 3 MS. MILLER: Objection. 4 THE WITNESS: I still... 5 MS. MILLER: What do you mean 6 by "know"? I mean, that's why I 7 objected to the question. 8 Do you mean know or know of? 9 MR. RESTAINO: Know. 10 MS. MILLER: Okay. 11 THE WITNESS: K-n-o-w? 12 MS. MILLER: Objection. 13 MR. RESTAINO: I'm sorry? 14 THE WITNESS: K-n-o-w? 15 MR. RESTAINO: Please. 16 MS. MILLER: I'm still 17 objecting to that because I don't know 18 what it means. 19 QUESTIONS BY MR. RESTAINO: 20 Q. If you saw Benjamin Neel at an 21 upcoming meeting, is it someone that you 22 would walk to and say, "Ben, how you doing?" 23 and shake his hand? 24 A. No. 25 Q. Okay. Do you know of</p>	<p style="text-align: right;">Page 32</p> <p>1 fellows at the center completed their 2 mandatory two years of research training in 3 my laboratory, and that's when I first met 4 Dr. Saenz. 5 Q. Okay. And number 9 is the 6 expert report of Dr. Saenz. 7 Have you reviewed her expert 8 report? 9 A. Yes. 10 Q. In its totality? 11 MS. MILLER: Objection. 12 QUESTIONS BY MR. RESTAINO: 13 Q. Let me rephrase. 14 Did you read the entire report 15 versus skimming it? 16 A. Two very different questions. 17 Q. Did you read her entire report? 18 A. No. 19 And now that we've defined in 20 its totality, I can perhaps go back and amend 21 my answers. 22 I generally skim all of these 23 documents. It's extraordinarily difficult 24 and time-consuming to read every word in 25 their totality.</p>
<p style="text-align: right;">Page 31</p> <p>1 Dr. Benjamin Neel in the professional sense? 2 A. Yes. 3 Q. And you read his deposition and 4 their exhibits? 5 A. Yes. 6 Q. And also on number 7 on that 7 list is the expert report. 8 Did you read the expert report 9 of Dr. Benjamin Neel in its totality? 10 MS. MILLER: Objection. 11 THE WITNESS: Yes. 12 QUESTIONS BY MR. RESTAINO: 13 Q. The number 2 on the list is a 14 Cheryl, and the last name is S-a-e-n-z, and 15 I'm not sure how it's pronounced. 16 A. Saenz. 17 Q. Do you know Cheryl Saenz in the 18 sense of walking up to her, shaking her hand, 19 saying "hi"? 20 A. Yes. 21 Q. Okay. And how do you know her? 22 A. I've known her for many years 23 when she was a GYN oncology fellow at the 24 Memorial Sloan Kettering Cancer Center. 25 Well, she and indeed all of the GYN oncology</p>	<p style="text-align: right;">Page 33</p> <p>1 Q. I understand. Thank you. 2 Number 3 on the list is the 3 deposition of Ie-Ming Shih, S-h-i-h. 4 Do you know Dr. Shih? 5 A. Yes. 6 Q. And did you skim his deposition 7 or read every question and every answer? 8 A. I skimmed his -- I'm assuming 9 we're talking about deposition transcript. 10 Yes. 11 Q. Okay. And number 10 is the 12 expert report of Dr. Shih, and same question: 13 Did you read the entire report? 14 A. I skimmed it. 15 Q. Okay. Attached to the report 16 was a study report representative of a 17 histopathological study that Dr. Shih has 18 performed. 19 Did you read that study report 20 also? 21 MS. MILLER: Objection. 22 THE WITNESS: I skimmed it in 23 an unusually cursory fashion. 24 QUESTIONS BY MR. RESTAINO: 25 Q. Did you read -- because I do</p>

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<p style="text-align: right;">Page 34</p> <p>1 not see it on here but within your expert 2 report. 3 You read Dr. Saed's expert 4 report, correct? 5 MS. MILLER: Well, this is the 6 supplemental list, so you wouldn't see 7 it on here. 8 MR. RESTAINO: Yes. 9 MS. MILLER: Do you want to go 10 back to his original materials relied 11 on now? 12 MR. RESTAINO: Don't think we 13 need to. Just want to know if he's 14 read Dr. Saed's report. 15 THE WITNESS: No, we're just 16 using a lot of names. I'm sorry. 17 Dr. Saed, yes, I read his 18 expert report, yes. 19 QUESTIONS BY MR. RESTAINO: 20 Q. And he's had his deposition 21 taken a couple of times, correct? 22 A. I am familiar with two 23 deposition transcripts, two separate 24 documents, which I would infer amounted to 25 two depositions.</p>	<p style="text-align: right;">Page 36</p> <p>1 you refer to the materials considered 2 in your report. 3 Do you have this? Do you want 4 it? 5 THE WITNESS: Sure. 6 MS. MILLER: Do you have the 7 report? 8 Can I give him a copy of the 9 report, or are you going to mark it? 10 MR. RESTAINO: Did I not give 11 him the report yet? 12 MS. MILLER: No. 13 MR. RESTAINO: Then let's do 14 that. 15 MS. MILLER: So... 16 (Boyd Exhibit 5 marked for 17 identification.) 18 QUESTIONS BY MR. RESTAINO: 19 Q. Previously marked as Exhibit 5 20 is a copy of your expert report. 21 MS. MILLER: And this has -- 22 what's attached to this? Because I 23 see you did the CV separately. 24 I'm confused. This also has a 25 CV? Oh, no, this is mine.</p>
<p style="text-align: right;">Page 35</p> <p>1 Q. Understood. Thank you. 2 Doctor, looking at the 3 supplemental materials considered, number 1 4 through 15, including deposition transcripts 5 and expert reports, these are all 6 individuals' deposition transcripts, exhibits 7 and expert reports for experts on behalf of 8 Johnson & Johnson, correct? 9 A. Yes, I believe so. 10 I'm sorry, I still have a 11 little trouble distinguishing the legal 12 representation from the corporation, but, 13 yes. 14 Q. And if at any time you're 15 unsure, then please ask, and the attorneys 16 present will try to straighten it out so that 17 you have a full understanding. 18 Other than Dr. Saed, his 19 deposition testimony and his expert report, 20 have you reviewed any of the expert reports 21 written by any of the other experts on behalf 22 of the plaintiffs? 23 MS. MILLER: I would refer you 24 to the materials considered. You said 25 it wasn't a memory test, so why don't</p>	<p style="text-align: right;">Page 37</p> <p>1 It's just the report. 2 MR. RESTAINO: It is just the 3 report. 4 MS. MILLER: Does it include 5 the materials considered? 6 THE WITNESS: I'm seeing on 7 page 25 materials considered, yeah. 8 MS. MILLER: Go ahead. 9 Is there a question pending, or 10 do you want to ask it again since 11 we -- 12 QUESTIONS BY MR. RESTAINO: 13 Q. I'll ask it again now that they 14 have it in front of you. 15 With this available to refresh 16 your memory, do you recall reading, other 17 than for Dr. Saed, any of the expert reports 18 for the plaintiffs' experts in this regard? 19 A. Vaguely. 20 Q. Okay. So, for example, 21 number 9 is the expert report of Daniel L. 22 Clarke, with an E, hyphen, Pearson. 23 Do you know Dr. Clarke-Pearson? 24 A. We've met. 25 Q. Did you meet when you were at</p>

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<p style="text-align: right;">Page 38</p> <p>1 University of North Carolina?</p> <p>2 A. I never -- well, our employment</p> <p>3 at the University of North Carolina didn't</p> <p>4 overlap, so, no.</p> <p>5 Q. Okay. In fact, you've</p> <p>6 coauthored a paper with Dr. Clarke-Pearson</p> <p>7 titled "Mutation of the P53 Tumor-Suppressor</p> <p>8 Gene is Not a Feature of Endometrial</p> <p>9 Hyperplasias."</p> <p>10 Does that sound familiar?</p> <p>11 A. I'll take your word for it.</p> <p>12 Q. Okay. Dr. Clarke-Pearson is a</p> <p>13 gynecological oncologist; is that your</p> <p>14 understanding?</p> <p>15 A. Until retirement, yes.</p> <p>16 Q. Okay. Well, he's still a</p> <p>17 gynecological oncologist, not practicing,</p> <p>18 correct?</p> <p>19 MS. MILLER: Objection.</p> <p>20 MR. RESTAINO: I'll withdraw</p> <p>21 the question.</p> <p>22 QUESTIONS BY MR. RESTAINO:</p> <p>23 Q. Doctor, are you an expert in</p> <p>24 gynecology?</p> <p>25 MS. MILLER: Objection.</p>	<p style="text-align: right;">Page 40</p> <p>1 the witness, please?</p> <p>2 MS. MILLER: I don't think that</p> <p>3 was coaching the witness.</p> <p>4 MR. RESTAINO: Okay. Well, you</p> <p>5 know what? It really doesn't matter</p> <p>6 what you think; it's what the Federal</p> <p>7 Rules say. The word "objection"</p> <p>8 works.</p> <p>9 THE WITNESS: I'm sorry, could</p> <p>10 you repeat the question?</p> <p>11 QUESTIONS BY MR. RESTAINO:</p> <p>12 Q. Sure.</p> <p>13 For purpose of developing your</p> <p>14 opinions in this litigation, did you not want</p> <p>15 to see what Dr. Clarke-Pearson had to say on</p> <p>16 the matter?</p> <p>17 MS. MILLER: Objection.</p> <p>18 THE WITNESS: I'm sorry, I just</p> <p>19 find that question very convoluted and</p> <p>20 difficult to answer.</p> <p>21 QUESTIONS BY MR. RESTAINO:</p> <p>22 Q. Okay. Do you know if</p> <p>23 Dr. Clarke-Pearson is still practicing?</p> <p>24 A. Well, for the third time, my</p> <p>25 understanding is that he's retired.</p>
<p style="text-align: right;">Page 39</p> <p>1 THE WITNESS: I do not hold</p> <p>2 myself out to be an expert in</p> <p>3 gynecology.</p> <p>4 QUESTIONS BY MR. RESTAINO:</p> <p>5 Q. Do you hold yourself out to be</p> <p>6 an expert in medical oncology?</p> <p>7 MS. MILLER: Objection.</p> <p>8 THE WITNESS: No.</p> <p>9 QUESTIONS BY MR. RESTAINO:</p> <p>10 Q. Dr. Clarke-Pearson is a</p> <p>11 gynecological oncologist, correct?</p> <p>12 A. I would offer the same answer</p> <p>13 that I previously rendered. Before he</p> <p>14 retired, it's my understanding that he was a</p> <p>15 gynecologic oncologist, yes.</p> <p>16 Q. For purposes of developing</p> <p>17 opinions in this litigation, did you not want</p> <p>18 to see what Dr. Clarke-Pearson had to say on</p> <p>19 the matter?</p> <p>20 MS. MILLER: Objection.</p> <p>21 I don't even know what you mean</p> <p>22 by that.</p> <p>23 If you do, you can answer.</p> <p>24 MR. RESTAINO: Jessica, can we</p> <p>25 just say "objection" without coaching</p>	<p style="text-align: right;">Page 41</p> <p>1 Q. Do you know if he's retired as</p> <p>2 the chair while still practicing?</p> <p>3 A. Could you clarify the chair of</p> <p>4 what and practicing what, please?</p> <p>5 Q. Well, do you understand that he</p> <p>6 was the chairman of gynecologic oncology</p> <p>7 there at University of North Carolina?</p> <p>8 A. No, he was not.</p> <p>9 Q. What was his position?</p> <p>10 A. Chair of the department of</p> <p>11 obstetrics and gynecology at the University</p> <p>12 of North Carolina.</p> <p>13 Q. Do you know if he's retired as</p> <p>14 chair of that position?</p> <p>15 A. That's my understanding, yes.</p> <p>16 Q. But do you know if he's stopped</p> <p>17 the practice of medicine?</p> <p>18 A. He never practiced medicine.</p> <p>19 He was a gynecologic oncologist. They're</p> <p>20 typically considered surgeons.</p> <p>21 Q. And in order to be a surgeon,</p> <p>22 one has to be licensed as a medical doctor,</p> <p>23 which by definition entails medicine; is that</p> <p>24 correct?</p> <p>25 MS. MILLER: Objection.</p>

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<p style="text-align: right;">Page 42</p> <p>1 THE WITNESS: The practice of 2 surgery is the practice of medicine, 3 I'll agree. 4 QUESTIONS BY MR. RESTAINO: 5 Q. Okay. Now, if you're not an 6 expert in gynecology and you're not an expert 7 in gynecological oncology, and you know a 8 Dr. Clarke-Pearson, who is a gynecological 9 oncologist, did you not have any interest in 10 ascertaining what his opinions were in this 11 litigation regarding talc and ovarian cancer? 12 MS. MILLER: Objection. 13 This misstates his testimony. 14 I mean, this question is extremely 15 misleading. I'm sorry, I know you 16 don't want me to object -- 17 MR. RESTAINO: Jessica, let me 18 help you. O-b-j-e-c-t-i-o-n. Do you 19 need me to write that on a piece of 20 paper and put it in front of you? 21 MS. MILLER: Do you need me to 22 write on a piece of paper how to ask 23 fair questions? 24 That was not a fair question. 25 He told you he read the guy's expert</p>	<p style="text-align: right;">Page 44</p> <p>1 opinions are in this litigation? 2 MS. MILLER: Objection. 3 THE WITNESS: I respectfully 4 request that you not yell at me. 5 QUESTIONS BY MR. RESTAINO: 6 Q. Doctor, do you know what 7 Dr. Clarke-Pearson's objections are in this 8 litigation -- his opinions are in this 9 litigation? 10 A. Not really. 11 Q. Do you know Arch Carson, MD, 12 Ph.D., physician, toxicologist, out of the 13 University of Texas? 14 A. I'm sorry, are we reading from 15 somewhere? 16 Q. My questions. 17 A. Something that I have? 18 Q. No. 19 There's a plaintiff attorney 20 {sic} by the name of Arch Carson, MD, Ph.D. 21 MS. MILLER: Objection. 22 MR. RESTAINO: A physician 23 toxicologist. 24 MS. MILLER: You said he's an 25 attorney. Is he an attorney for you</p>
<p style="text-align: right;">Page 43</p> <p>1 report -- 2 MR. RESTAINO: The word 3 "objection" then covers it -- 4 MS. MILLER: -- and you keep 5 suggesting this -- 6 MR. RESTAINO: And the judge 7 will decide what's fair and what's not 8 fair. 9 MS. MILLER: Okay. 10 MR. RESTAINO: We may have a 11 professional disagreement, and you say 12 "objection." And I look at it and 13 think, okay, let me rephrase it. 14 MS. MILLER: You didn't 15 rephrase it. 16 MR. RESTAINO: Let's not do 17 that all day. 18 MS. MILLER: You've done it 19 three times, the same objectionable 20 question, so I don't -- 21 MR. RESTAINO: Because he's not 22 answering it. 23 QUESTIONS BY MR. RESTAINO: 24 Q. Doctor, do you have any 25 interest in what Dr. Clarke-Pearson's</p>	<p style="text-align: right;">Page 45</p> <p>1 guys, too? 2 MR. RESTAINO: He's a physician 3 toxicologist out of the University of 4 Texas, a plaintiff expert. 5 QUESTIONS BY MR. RESTAINO: 6 Q. Do you know Dr. Carson or know 7 of him? 8 A. Neither. 9 Q. Are you an expert in 10 toxicology? 11 A. No. 12 Q. Did you have any interest in 13 seeing what a plaintiff's expert in 14 toxicology's opinions were in this 15 litigation? 16 MS. MILLER: Objection. 17 THE WITNESS: I think it's fair 18 to say that with an unlimited amount 19 of time, I would have had some degree 20 of curiosity and interest in reading 21 every document associated with this 22 litigation. 23 But with two full-time jobs, a 24 family and the time constraints that 25 we're under, I simply have to focus on</p>

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<p style="text-align: right;">Page 46</p> <p>1 what I think is most relevant to my</p> <p>2 role in this litigation, which is</p> <p>3 offering opinions on Dr. Saed's work</p> <p>4 specifically and more generally on</p> <p>5 biological plausibility of the</p> <p>6 relationship of the -- the</p> <p>7 hypothesized association of perineal</p> <p>8 use of talc and ovarian cancer.</p> <p>9 QUESTIONS BY MR. RESTAINO:</p> <p>10 Q. And I appreciate, understand</p> <p>11 time constraints we all function under, but</p> <p>12 under the supplemental materials considered</p> <p>13 list, there are 15 documents, including</p> <p>14 deposition and exhibits and expert reports of</p> <p>15 multiple defense experts.</p> <p>16 You had the time to read those</p> <p>17 but not the plaintiff expert reports; is that</p> <p>18 true?</p> <p>19 MS. MILLER: Objection.</p> <p>20 Mischaracterizes his testimony.</p> <p>21 THE WITNESS: I believe it's</p> <p>22 fair to say I had time to at the very</p> <p>23 least cursorily skim all of the</p> <p>24 materials considered to one degree or</p> <p>25 another.</p>	<p style="text-align: right;">Page 48</p> <p>1 QUESTIONS BY MR. RESTAINO:</p> <p>2 Q. Okay. Do you know or have you</p> <p>3 heard of Dr. Jack Siemiatycki,</p> <p>4 S-i-e-m-i-a-t-y-c-k-i?</p> <p>5 A. I don't know the doctor.</p> <p>6 Q. Okay. Did you review any</p> <p>7 epidemiological report written by any of the</p> <p>8 plaintiffs' epidemiological experts?</p> <p>9 A. I don't recall.</p> <p>10 Q. Do you know or know of</p> <p>11 Dr. Judith Wolf, MD, a gynecological</p> <p>12 oncologist with the National Ovarian Cancer</p> <p>13 Coalition?</p> <p>14 A. I'm sorry, that's a complicated</p> <p>15 question. The National Ovarian Cancer</p> <p>16 Coalition is a foundation.</p> <p>17 I know of Dr. Judith Wolf. To</p> <p>18 the best of my ability to recall, she, at</p> <p>19 least at some point in her career, has worked</p> <p>20 as a gynecologic oncologist at the MD</p> <p>21 Anderson Cancer Center.</p> <p>22 Q. Have you ever coauthored any</p> <p>23 publications with Dr. Wolf?</p> <p>24 A. I cannot say with certainty.</p> <p>25 I've coauthored lots of papers with lots of</p>
<p style="text-align: right;">Page 47</p> <p>1 QUESTIONS BY MR. RESTAINO:</p> <p>2 Q. Did you skim the expert report</p> <p>3 of Ellen Blair Smith, a physician,</p> <p>4 gynecologist, oncologist?</p> <p>5 A. I don't remember doing so.</p> <p>6 Q. Okay. Do you recall -- or do</p> <p>7 you know Ellen Blair Smith, Dr. Smith?</p> <p>8 A. No.</p> <p>9 Q. In 2017, did you coauthor a</p> <p>10 paper titled "Multi-Disciplinary Summit on</p> <p>11 Genetic Services for Women with Gynecological</p> <p>12 Cancers: A Society of Gynecologic Oncology</p> <p>13 White Paper"?</p> <p>14 Do you recall that publication?</p> <p>15 A. I do.</p> <p>16 Q. And do you recall Dr. Smith</p> <p>17 being a coauthor with you on that paper?</p> <p>18 A. No.</p> <p>19 Q. Do you know that Dr. Smith is a</p> <p>20 gynecological oncologist?</p> <p>21 MS. MILLER: Objection.</p> <p>22 He said he doesn't know who she</p> <p>23 is.</p> <p>24 THE WITNESS: I don't know who</p> <p>25 she is.</p>	<p style="text-align: right;">Page 49</p> <p>1 coauthors, and some I remember, and some I</p> <p>2 don't.</p> <p>3 Q. I understand.</p> <p>4 Dr. Judith Zelikoff,</p> <p>5 Z-e-l-i-c-o-f-f, is a professor of at NYU.</p> <p>6 Do you know Dr. Zelikoff?</p> <p>7 A. No.</p> <p>8 Q. And Dr. Laura Plunkett, Ph.D.,</p> <p>9 is a pharmacologist, toxicologist.</p> <p>10 Do you know Dr. Plunkett?</p> <p>11 A. No.</p> <p>12 Q. Are you an expert in</p> <p>13 pharmacology?</p> <p>14 MS. MILLER: Objection.</p> <p>15 THE WITNESS: No.</p> <p>16 QUESTIONS BY MR. RESTAINO:</p> <p>17 Q. Did you have any interest in</p> <p>18 seeing what plaintiff expert pharmacologist</p> <p>19 opinions were regarding talc and ovarian</p> <p>20 cancer?</p> <p>21 MS. MILLER: Objection.</p> <p>22 THE WITNESS: Again, that's a</p> <p>23 very difficult question to answer.</p> <p>24 I'm interested in many things.</p> <p>25</p>

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<p style="text-align: right;">Page 50</p> <p>1 QUESTIONS BY MR. RESTAINO: 2 Q. Did you not have the interest, 3 though, to pick up her expert report and read 4 it? 5 MS. MILLER: Objection. 6 THE WITNESS: I think interest 7 and time are two different things. 8 QUESTIONS BY MR. RESTAINO: 9 Q. Sarah Kane, MD, is a 10 pathologist up in the Boston area. 11 Do you know of Dr. Kane? 12 A. I've seen her name. 13 Q. And do you recall where you've 14 seen her name? 15 A. In some of the deposition 16 transcripts associated with this litigation. 17 Q. And did you read Dr. Kane's 18 report as an expert in pathology? 19 A. I skimmed it. 20 Q. Are you an expert in pathology? 21 A. No. 22 Q. Do you know Shawn Levy, 23 L-e-v-y, Ph.D., with the Genomics Services 24 Laboratory at the Hudson Alpha Institute for 25 Biotechnology?</p>	<p style="text-align: right;">Page 52</p> <p>1 QUESTIONS BY MR. RESTAINO: 2 Q. Do you know how many 3 publications on ovarian cancer Dr. Cramer has 4 in the peer-reviewed literature? 5 A. I'm sure I don't. 6 Q. Okay. Did you have any 7 interest in seeing what Dr. Cramer had to say 8 in the -- this litigation? 9 MS. MILLER: Objection. 10 THE WITNESS: I think it's fair 11 to say that I'm relatively familiar 12 with Dr. Cramer's work over the years. 13 I cannot say that I devoted a 14 substantial amount of time to 15 reviewing his opinion in this 16 particular context over the past 17 several months. 18 QUESTIONS BY MR. RESTAINO: 19 Q. Would you consider yourself an 20 expert in the epidemiology of ovarian cancer 21 and its associated risk factors? 22 MS. MILLER: Objection. 23 THE WITNESS: Again, a 24 difficult question to answer. I would 25 not consider myself an expert. I</p>
<p style="text-align: right;">Page 51</p> <p>1 A. No. 2 Q. And how about Sonal Singh, 3 S-i-n-g, {sic} MD, MPH, a medical 4 epidemiologist? 5 A. A medical epidemiologist? No. 6 Q. Daniel Cramer, MD, DSC, at 7 Brigham and Women's Hospital, also a 8 physician and epidemiologist. 9 Do you know Dan Cramer? 10 A. Yes. 11 Q. Do you know him to be a 12 professor of epidemiology at the Harvard 13 T.H. Chan School of Public Health? 14 A. I honestly can't say what his 15 current position is. 16 Q. Okay. Are you aware of 17 Dr. Cramer's work and publications pertaining 18 to ovarian cancer? 19 MS. MILLER: Objection. 20 THE WITNESS: I'm aware that 21 Dr. Cramer over many years has had an 22 interest, a research interest, in the 23 issue of an association with talc 24 exposure and the development of 25 ovarian cancer.</p>	<p style="text-align: right;">Page 53</p> <p>1 would say that I'm familiar with some 2 of the basic concepts of epidemiologic 3 aspects of ovarian cancer. 4 QUESTIONS BY MR. RESTAINO: 5 Q. Okay. If there were instances 6 regarding the epidemiological principles 7 associated with studies of ovarian cancer and 8 talc, would you defer to someone like Dan 9 Cramer as a medical epidemiologist? 10 MS. MILLER: Objection. 11 THE WITNESS: Defer in what 12 context? 13 QUESTIONS BY MR. RESTAINO: 14 Q. If you're not understanding 15 what the epidemiological principles may be, 16 would you defer to an epidemiologist? 17 MS. MILLER: Objection. 18 THE WITNESS: So your first 19 question was would I defer to 20 Dr. Cramer, and your second question 21 was to an epidemiologist? 22 QUESTIONS BY MR. RESTAINO: 23 Q. Yes. 24 A. Which one am I answering, 25 please?</p>

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<p style="text-align: right;">Page 54</p> <p>1 MS. MILLER: Well, they also 2 had different "ifs," so... 3 QUESTIONS BY MR. RESTAINO: 4 Q. If you're not understanding 5 what the epidemiological principles may be, 6 would you defer to an epidemiologist? 7 MS. MILLER: Objection. 8 Mischaracterizes his testimony. 9 THE WITNESS: I might defer to 10 anyone on any given day about any 11 given topic that had to do with a 12 field of inquiry in which I'm not an 13 expert. 14 QUESTIONS BY MR. RESTAINO: 15 Q. Okay. Are you an expert in the 16 epidemiological principle of effect 17 modification? 18 A. No. 19 Q. As such, would you defer to a 20 medical epidemiologist such as Dan Cramer to 21 explain effect modification and whatever role 22 it may have regarding talcum powder and 23 ovarian cancer? 24 MS. MILLER: Objection. 25 THE WITNESS: If I was indeed</p>	<p style="text-align: right;">Page 56</p> <p>1 Q. Okay. And who was that? 2 A. Ms. Miller. 3 Q. And have you talked with -- 4 worked with Ms. Miller in the past? 5 A. Prior to mid-December of 2018? 6 Q. Yes, sir. 7 A. No. 8 Q. Prior to your meeting with 9 Ms. Miller, had you conducted any original 10 research on your part to the association, if 11 any, between talcum powder and the 12 development of ovarian cancer? 13 MS. MILLER: Objection. 14 THE WITNESS: No. 15 QUESTIONS BY MR. RESTAINO: 16 Q. Prior to you meeting with 17 Ms. Miller in December of 2018, had you 18 lectured to any professional society -- and 19 by that I mean medical and/or scientific -- 20 regarding the association between talcum 21 powder and ovarian cancer? 22 A. No. 23 Q. Prior to your meeting with 24 Ms. Miller in December of 2018, had you 25 formulated an opinion regarding an</p>
<p style="text-align: right;">Page 55</p> <p>1 interested in an acute sense about 2 that particular issue, I would 3 probably approach someone that I knew 4 better than Dr. Cramer and certainly 5 perhaps closer to home. 6 QUESTIONS BY MR. RESTAINO: 7 Q. Okay. When were you first 8 contacted by any representative of Johnson & 9 Johnson to serve as an expert in this 10 litigation? 11 A. Could you repeat the question, 12 please? 13 Q. When you were first contacted 14 by any representative of Johnson & Johnson to 15 see if you would work as an expert witness in 16 this litigation? 17 MS. MILLER: Objection. 18 THE WITNESS: To my knowledge, 19 I've never been approached by a 20 representative of Johnson & Johnson. 21 QUESTIONS BY MR. RESTAINO: 22 Q. Were you ever -- when were you 23 approached by any attorney representing 24 Johnson & Johnson? 25 A. Mid-December of 2018.</p>	<p style="text-align: right;">Page 57</p> <p>1 association between talcum powder and ovarian 2 cancer? 3 A. Yes. 4 Q. And when did you develop that 5 opinion? 6 A. Over several decades. 7 Q. Going back to the 1990s or 8 early 2000s? 9 A. Hard to say, but I would 10 estimate that I may have been aware of 11 studies involving a possible association of 12 talc exposure and ovarian cancer as long ago 13 as the late '80s, early '90s, were such 14 studies to have existed. 15 Q. Okay. Prior to your meeting 16 with Ms. Miller in December of 2018, had you 17 formulated an opinion regarding risk factors 18 associated with the development of ovarian 19 cancer? 20 MS. MILLER: I'm going to have 21 to keep objecting to these questions. 22 He said he was contacted in 23 December 2018. He never said he met 24 with Ms. Miller in December of 2018, 25 and you've now embedded that into like</p>

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<p style="text-align: right;">Page 58</p> <p>1 three questions. 2 And I'm sorry if this is a 3 speaking objection, but that's just 4 not an accurate recitation of his 5 testimony. 6 MR. RESTAINO: Let me withdraw 7 the question. 8 QUESTIONS BY MR. RESTAINO: 9 Q. And relating back to the other 10 questions I asked you, did you, in December 11 of 2018, meet with Jessica Miller or talk 12 with her on the phone? 13 A. My memory is that our first 14 communication was e-mail. 15 Q. And -- 16 A. Subsequent communication was 17 telephone. 18 Q. Okay. So that would apply to 19 all your prior answers when I asked you 20 regarding meeting Ms. Miller? 21 A. I honestly don't remember the 22 questions and how meeting Ms. Miller had been 23 embedded in them. 24 Q. Okay. Prior to any 25 communication with any attorney representing</p>	<p style="text-align: right;">Page 60</p> <p>1 Q. Yes. 2 A. A clinical cancer geneticist 3 and a molecular diagnostician. 4 Q. And what do you mean when you 5 say "a clinical cancer geneticist"? 6 A. Well, cancer genetics, 7 clinical, the clinical implications of cancer 8 genetics, and the -- and the practice of 9 dealing with patients with genetic 10 predisposition to cancer, as well as a 11 clinical molecular diagnostics practice 12 wherein we examine the genetic architecture 13 of an individual patient's tumor in order to 14 perform precision cancer therapy. 15 Q. Okay. You're not a medical 16 doctor; is that correct? 17 A. That's correct. 18 Q. When you were studying either 19 undergrad or for your Ph.D., did you take 20 general anatomy? 21 A. Probably. 22 Q. Did you dissect a cadaver? 23 A. Human? 24 Q. Yes. 25 A. No.</p>
<p style="text-align: right;">Page 59</p> <p>1 Johnson & Johnson prior to January 1st of 2 2019, you had formulated an opinion regarding 3 talcum powder and ovarian cancer; is that 4 correct? 5 A. That's fair, yes. 6 Q. And what was the basis for that 7 opinion or opinions, if you recall? 8 A. Several decades of a rather 9 passive reading of the literature in general, 10 which given an interest in ovarian cancer is 11 quite typical in my scientists and 12 clinicians. I try to stay abreast of the 13 literature in all forms. 14 Q. Okay. Now, you received your 15 Ph.D. from North Carolina State University; 16 is that correct? 17 A. Yes. 18 Q. Would you describe yourself as 19 a cellular biologist? 20 A. No. 21 Q. How would you introduce 22 yourself to a fellow scientist or physician 23 at a meeting you first -- meet for the first 24 time? 25 A. Today?</p>	<p style="text-align: right;">Page 61</p> <p>1 Q. Have you ever studied through 2 dissection, textbook or virtual reality the 3 anatomy of the female genitourinary tract? 4 A. I would refer to it as the 5 female reproductive tract, but I think the 6 answer to your question is yes. 7 MR. RESTAINO: Okay. 8 MS. MILLER: Is this a good 9 time for break? We've been going an 10 hour. 11 MR. RESTAINO: Sure. 12 VIDEOGRAPHER: Off the record 13 at 10:02 a.m. 14 (Off the record at 10:02 a.m.) 15 VIDEOGRAPHER: We're back on 16 record at 10:14 a.m. 17 QUESTIONS BY MR. RESTAINO: 18 Q. Welcome back, Doctor. 19 A. Thank you. 20 Q. During the course of today 21 there are going to be some documents that 22 we'll refer to frequently. Your expert 23 report, that one you might want to keep, you 24 know, in one particular pile. And some of 25 the others, like CV and maybe an article that</p>

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<p style="text-align: right;">Page 62</p> <p>1 we just look at momentarily, I'll let you</p> <p>2 know, and you can just get it out of your</p> <p>3 way, if that helps.</p> <p>4 A. Excellent, thank you.</p> <p>5 Q. Now, we had discussed that</p> <p>6 prior to your communication of any sort with</p> <p>7 Ms. Miller, that you had some opinions</p> <p>8 regarding talc and ovarian cancer; is that</p> <p>9 correct?</p> <p>10 A. Yes.</p> <p>11 Q. As you sit here today, can you</p> <p>12 tell us what those opinions were?</p> <p>13 A. My opinion, generally speaking,</p> <p>14 was that the existing body of scientific</p> <p>15 evidence did not support a causal association</p> <p>16 between perineal talc exposure and the</p> <p>17 development of epithelial ovarian carcinoma.</p> <p>18 And, of course, we're speaking</p> <p>19 about many distinct diseases when we refer to</p> <p>20 EOC, but...</p> <p>21 Q. Did you have, at the time you</p> <p>22 held an opinion that the existing body of</p> <p>23 scientific evidence did not support a causal</p> <p>24 association, an opinion regarding the</p> <p>25 biologically plausible risk factors for</p>	<p style="text-align: right;">Page 64</p> <p>1 of the term is any factor, behavior,</p> <p>2 exposure, habit of lifestyle that</p> <p>3 either increases or decreases in a</p> <p>4 substantive fashion one's risk for</p> <p>5 ovarian cancer.</p> <p>6 QUESTIONS BY MR. RESTAINO:</p> <p>7 Q. Okay. Before we broke, I was</p> <p>8 asking if you had taken a general anatomy</p> <p>9 course or class regarding not only general</p> <p>10 anatomy but also the female reproductive</p> <p>11 tract, correct?</p> <p>12 Do you recall those questions?</p> <p>13 A. You're correct that I recall</p> <p>14 those questions.</p> <p>15 Q. Okay. As you sit here today,</p> <p>16 do you know what a woman's labia are,</p> <p>17 anatomically speaking?</p> <p>18 A. Are you referring to the</p> <p>19 components of the vulva?</p> <p>20 Q. To however you would define a</p> <p>21 woman's labia.</p> <p>22 A. The labia majoras and labia</p> <p>23 minoras I would consider components of the</p> <p>24 external female genitalia, typically referred</p> <p>25 to in aggregate as the vulva.</p>
<p style="text-align: right;">Page 63</p> <p>1 ovarian cancer?</p> <p>2 MS. MILLER: Objection.</p> <p>3 THE WITNESS: I'm sorry, but I</p> <p>4 just can't follow that question.</p> <p>5 QUESTIONS BY MR. RESTAINO:</p> <p>6 Q. Did you --</p> <p>7 A. Maybe break it down.</p> <p>8 Q. Yes.</p> <p>9 Did you have an opinion, prior</p> <p>10 to January 1, 2019, regarding biologically</p> <p>11 plausible risk factors for the development of</p> <p>12 ovarian cancer?</p> <p>13 A. Oh, I'm sorry, yes.</p> <p>14 Q. Okay. Can you define for us as</p> <p>15 we go forward in the day your definition of a</p> <p>16 risk factor?</p> <p>17 A. I missed a couple words there</p> <p>18 in the middle of that question.</p> <p>19 Q. Just going forward for the</p> <p>20 course of the day, I want to use your</p> <p>21 definition. So can you define for us your</p> <p>22 definition of a risk factor, specifically as</p> <p>23 it relates to ovarian cancer?</p> <p>24 MS. MILLER: Objection.</p> <p>25 THE WITNESS: My understanding</p>	<p style="text-align: right;">Page 65</p> <p>1 Q. Okay. And collectively as the</p> <p>2 vulva, do you have an opinion as to whether</p> <p>3 the vulva exists as a barrier between the</p> <p>4 external environment and the vagina?</p> <p>5 MS. MILLER: Objection.</p> <p>6 THE WITNESS: I'm not prepared</p> <p>7 to testify about anatomical barriers</p> <p>8 between the environment and anything</p> <p>9 else.</p> <p>10 QUESTIONS BY MR. RESTAINO:</p> <p>11 Q. Okay. Would you defer to a</p> <p>12 gynecologist or a physician in that regard?</p> <p>13 MS. MILLER: Objection.</p> <p>14 THE WITNESS: If I was</p> <p>15 interested in pursuing such a</p> <p>16 question, it's much more likely that I</p> <p>17 would start pulling out textbooks and</p> <p>18 scientific papers on the topic.</p> <p>19 QUESTIONS BY MR. RESTAINO:</p> <p>20 Q. Okay. As you sit here today,</p> <p>21 do you have an opinion as to whether the</p> <p>22 vulva, as defined by yourself, closes off the</p> <p>23 vagina from the external environment?</p> <p>24 A. Again --</p> <p>25 MS. MILLER: Objection. Asked</p>

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<p style="text-align: right;">Page 66</p> <p>1 and answered.</p> <p>2 Please give me a second to</p> <p>3 object, even though my objections --</p> <p>4 thank you.</p> <p>5 THE WITNESS: Again, I'm not</p> <p>6 prepared to offer an opinion on that</p> <p>7 topic.</p> <p>8 QUESTIONS BY MR. RESTAINO:</p> <p>9 Q. Have you ever diagnosed a woman</p> <p>10 with ovarian cancer?</p> <p>11 A. No.</p> <p>12 Q. And as a Ph.D. scientist, is it</p> <p>13 correct in saying that you do not have the --</p> <p>14 you don't have the privileges to treat women</p> <p>15 with cancer?</p> <p>16 MS. MILLER: Objection.</p> <p>17 THE WITNESS: That's a</p> <p>18 complicated question.</p> <p>19 I oversee a clinical, which is</p> <p>20 to say CLIA-certified and</p> <p>21 CAP-accredited, molecular diagnostics</p> <p>22 laboratory wherein we subject ovarian</p> <p>23 cancers, tumor tissues themselves, to</p> <p>24 a rather complex next generation</p> <p>25 sequencing-based interrogation of the</p>	<p style="text-align: right;">Page 68</p> <p>1 opposed to traditional chemotherapy agents.</p> <p>2 But to the extent that anything is prescribed</p> <p>3 to the patient, that would be the oncologist,</p> <p>4 correct.</p> <p>5 Q. Same answer if I was to ask you</p> <p>6 if you were licensed to perform surgery on a</p> <p>7 woman?</p> <p>8 A. I'm not an MD.</p> <p>9 Q. Will you be offering any</p> <p>10 opinions regarding strengths and/or</p> <p>11 weaknesses of any of the epidemiological</p> <p>12 studies looking at the association between</p> <p>13 talcum powder and ovarian cancer?</p> <p>14 MS. MILLER: I just want to</p> <p>15 look at that question.</p> <p>16 Objection.</p> <p>17 THE WITNESS: I was asked to</p> <p>18 render opinions here today on the</p> <p>19 veracity of Dr. Saed's work, his</p> <p>20 testimony, his expert report</p> <p>21 specifically, and generally perhaps on</p> <p>22 biological plausibility, getting us</p> <p>23 from association to causality in this</p> <p>24 particular litigation.</p> <p>25 MR. RESTAINO: And this is one</p>
<p style="text-align: right;">Page 67</p> <p>1 genomic architecture of aforementioned</p> <p>2 tumor in an attempt to link specific</p> <p>3 genetic mutations in that tumor to</p> <p>4 specific precision therapeutics.</p> <p>5 And the end result of that</p> <p>6 clinical laboratory process is the</p> <p>7 generation of what's known as</p> <p>8 molecular pathology report, which is</p> <p>9 then returned to the ordering</p> <p>10 oncologist, which allows he or she to</p> <p>11 make a hopefully precision therapeutic</p> <p>12 treatment determination.</p> <p>13 QUESTIONS BY MR. RESTAINO:</p> <p>14 Q. And if that -- was there a</p> <p>15 period?</p> <p>16 A. Yes.</p> <p>17 Q. Okay. And if the organized</p> <p>18 oncologist decides to prescribe a specific</p> <p>19 regimen of chemotherapy, he or she would be</p> <p>20 licensed to do that and not yourself; is that</p> <p>21 correct?</p> <p>22 A. Well, let's back up a little</p> <p>23 bit. Actually we were talking about</p> <p>24 precision therapeutics, which typically are</p> <p>25 small molecules or monoclonal antibodies as</p>	<p style="text-align: right;">Page 69</p> <p>1 of those times when I'll say move to</p> <p>2 strike as unresponsive.</p> <p>3 QUESTIONS BY MR. RESTAINO:</p> <p>4 Q. And the question is: Will you</p> <p>5 be offering any opinions regarding strengths</p> <p>6 and/or weaknesses of any of the</p> <p>7 epidemiological studies looking at the</p> <p>8 association between talcum powder and the</p> <p>9 development of ovarian cancer?</p> <p>10 MS. MILLER: Objection.</p> <p>11 THE WITNESS: I will not</p> <p>12 voluntarily be offering any opinions.</p> <p>13 I will do my best to answer any</p> <p>14 question you ask me. Some of them --</p> <p>15 many of them, perhaps, may be that I'm</p> <p>16 not comfortable or qualified to answer</p> <p>17 that question.</p> <p>18 Some I may answer.</p> <p>19 QUESTIONS BY MR. RESTAINO:</p> <p>20 Q. Okay. Do you consider yourself</p> <p>21 an expert in mineralogy?</p> <p>22 A. No.</p> <p>23 Q. And an expert in geology?</p> <p>24 A. No.</p> <p>25 Q. Do you consider yourself an</p>

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<p>1 expert in talcum powder?</p> <p>2 MS. MILLER: Objection.</p> <p>3 THE WITNESS: I can honestly</p> <p>4 say I've never met an expert in talcum</p> <p>5 powder.</p> <p>6 QUESTIONS BY MR. RESTAINO:</p> <p>7 Q. Do you have a basic</p> <p>8 understanding of what talcum powder is?</p> <p>9 A. Yes.</p> <p>10 Q. And what is that understanding?</p> <p>11 A. Finely ground talc.</p> <p>12 Q. Would you agree that it is a</p> <p>13 mineral composed of various elements?</p> <p>14 MS. MILLER: Objection.</p> <p>15 THE WITNESS: Could you restate</p> <p>16 the question?</p> <p>17 QUESTIONS BY MR. RESTAINO:</p> <p>18 Q. Would you agree that it is a</p> <p>19 mineral composed of various elements?</p> <p>20 A. What is "it"?</p> <p>21 Q. Talcum powder.</p> <p>22 A. Well, to the extent that talcum</p> <p>23 powder is finely ground talc, I would agree</p> <p>24 that talc is a mineral composed, as all</p> <p>25 minerals are, of particular molecules.</p>	<p>1 40 years to the last time I looked at a</p> <p>2 periodic table. Perhaps silicon.</p> <p>3 Q. Can you explain to us what a</p> <p>4 ligand is, l-i-g-a-n-d?</p> <p>5 A. In my mind, a ligand is any</p> <p>6 substance or molecule that interacts with a</p> <p>7 receptor in a very general sense.</p> <p>8 Q. Do you find ligands attached to</p> <p>9 other compounds? For example, metals?</p> <p>10 MS. MILLER: Objection.</p> <p>11 THE WITNESS: That's such an</p> <p>12 extraordinarily general question, I</p> <p>13 just...</p> <p>14 QUESTIONS BY MR. RESTAINO:</p> <p>15 Q. Let me rephrase it then.</p> <p>16 Are you aware of any ligands</p> <p>17 that by themselves are injected into the</p> <p>18 human body for whatever reason?</p> <p>19 MS. MILLER: Objection.</p> <p>20 THE WITNESS: Again, just -- I</p> <p>21 can't even begin to answer that</p> <p>22 question. It's overly broad.</p> <p>23 QUESTIONS BY MR. RESTAINO:</p> <p>24 Q. What purpose does a ligand</p> <p>25 have, chemically speaking?</p>
Page 71	Page 73
<p>1 Q. Magnesium?</p> <p>2 A. That's one.</p> <p>3 Q. Silicon?</p> <p>4 A. That's another.</p> <p>5 Q. Oxygen?</p> <p>6 A. That's another.</p> <p>7 Q. Hydrogen?</p> <p>8 A. Those are them.</p> <p>9 Q. Would you agree that talc is</p> <p>10 not a mineral -- excuse me, is not a metal?</p> <p>11 A. With all due respect, that's a</p> <p>12 trick question.</p> <p>13 Q. How so?</p> <p>14 MS. MILLER: Objection.</p> <p>15 QUESTIONS BY MR. RESTAINO:</p> <p>16 Q. How can I make the question any</p> <p>17 easier for you without trying to be --</p> <p>18 without any component of tricking?</p> <p>19 A. Talc, as we just discussed,</p> <p>20 consists of multiple elements. One or more</p> <p>21 of those elements from a chemical</p> <p>22 perspective, for example, if one examined the</p> <p>23 periodic table, may be considered a metal.</p> <p>24 Q. Which one?</p> <p>25 A. And I'm thinking now back</p>	<p>1 MS. MILLER: Objection.</p> <p>2 THE WITNESS: Ligands don't</p> <p>3 have purposes.</p> <p>4 QUESTIONS BY MR. RESTAINO:</p> <p>5 Q. They don't?</p> <p>6 MS. MILLER: Is that a</p> <p>7 question?</p> <p>8 MR. RESTAINO: That's a</p> <p>9 question: They don't?</p> <p>10 MS. MILLER: Okay. I'm</p> <p>11 objecting to that then.</p> <p>12 THE WITNESS: I -- you know, I</p> <p>13 hesitate to delve into a debate</p> <p>14 involving syntax or metaphysical</p> <p>15 arguments, but I think humans have a</p> <p>16 purpose generally. I think inert</p> <p>17 compounds are elements.</p> <p>18 QUESTIONS BY MR. RESTAINO:</p> <p>19 Q. I'm sorry, was that a period?</p> <p>20 A. No.</p> <p>21 Q. Oh, okay.</p> <p>22 A. Generally don't have a purpose</p> <p>23 in terms of cognitive function.</p> <p>24 Q. Going back to the periodic</p> <p>25 table, are you familiar with the element</p>

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<p style="text-align: right;">Page 74</p> <p>1 gadolinium?</p> <p>2 MS. MILLER: Objection.</p> <p>3 Is this a chemistry class?</p> <p>4 MS. SHARKO: Wrong litigation,</p> <p>5 John.</p> <p>6 MS. MILLER: I know. Yeah.</p> <p>7 It's the wrong litigation; it's the</p> <p>8 wrong expert.</p> <p>9 Is he here as a chemistry</p> <p>10 expert? Because I don't see that</p> <p>11 anywhere in his report.</p> <p>12 QUESTIONS BY MR. RESTAINO:</p> <p>13 Q. Doctor, are you familiar with</p> <p>14 the element gadolinium?</p> <p>15 A. I do not hold myself out as a</p> <p>16 chemist, a mineralogist, a geologist.</p> <p>17 Q. As a scientist, do you know if</p> <p>18 gadolinium had been injected into the human</p> <p>19 body without a ligand around it?</p> <p>20 A. I'm sure it can. I...</p> <p>21 Q. Do you have a basic --</p> <p>22 MS. MILLER: He's like in the</p> <p>23 middle of forming a word, and you're</p> <p>24 interrupting him.</p> <p>25 MR. RESTAINO: Oh, I'm sorry, I</p>	<p style="text-align: right;">Page 76</p> <p>1 any Johnson & Johnson talcum powder product?</p> <p>2 A. Could you please repeat the</p> <p>3 question?</p> <p>4 Q. Do you have an opinion as to</p> <p>5 whether or not there is asbestos present in</p> <p>6 any Johnson & Johnson talcum powder product?</p> <p>7 A. No.</p> <p>8 Q. Do you have an opinion as to</p> <p>9 whether or not there is any fibrous talc</p> <p>10 present in any Johnson & Johnson talcum</p> <p>11 powder?</p> <p>12 A. Again, if we're referring to</p> <p>13 Johnson's baby powder, the answer would be</p> <p>14 no.</p> <p>15 Q. Do you know if there are any</p> <p>16 other suspected carcinogens known to be</p> <p>17 within the fragrant chemicals that can be</p> <p>18 found in Johnson & Johnson baby powder --</p> <p>19 MS. MILLER: Objection.</p> <p>20 QUESTIONS BY MR. RESTAINO:</p> <p>21 Q. -- or talcum powder?</p> <p>22 MS. MILLER: Objection.</p> <p>23 THE WITNESS: I have no</p> <p>24 opinion.</p> <p>25</p>
<p style="text-align: right;">Page 75</p> <p>1 heard a period there.</p> <p>2 MS. MILLER: His mouth was</p> <p>3 open.</p> <p>4 THE WITNESS: I think</p> <p>5 theoretically it's possible to inject</p> <p>6 anything into the human body.</p> <p>7 QUESTIONS BY MR. RESTAINO:</p> <p>8 Q. Okay. Is it safe to inject</p> <p>9 gadolinium without a ligand into the human</p> <p>10 body?</p> <p>11 MS. MILLER: Objection.</p> <p>12 THE WITNESS: I can't answer</p> <p>13 that.</p> <p>14 QUESTIONS BY MR. RESTAINO:</p> <p>15 Q. Do you have a basic</p> <p>16 understanding of what asbestos is?</p> <p>17 A. I have a very basic</p> <p>18 understanding, yes. Not a detailed</p> <p>19 understanding as, again, I'm neither a</p> <p>20 mineralogist nor a geologist nor a chemist.</p> <p>21 Q. Have you ever studied the</p> <p>22 effect of asbestos in the human body?</p> <p>23 A. No.</p> <p>24 Q. Do you have an opinion as to</p> <p>25 whether or not there's asbestos present in</p>	<p style="text-align: right;">Page 77</p> <p>1 QUESTIONS BY MR. RESTAINO:</p> <p>2 Q. Were you ever asked to look</p> <p>3 into whether or not these substances may be</p> <p>4 in Johnson & Johnson talcum powder?</p> <p>5 MS. MILLER: Objection.</p> <p>6 THE WITNESS: No.</p> <p>7 QUESTIONS BY MR. RESTAINO:</p> <p>8 Q. Were you ever asked to look</p> <p>9 into whether or not there are any heavy</p> <p>10 metals present in Johnson & Johnson's talcum</p> <p>11 powder?</p> <p>12 A. No.</p> <p>13 Q. Did you ask to see if Johnson &</p> <p>14 Johnson had any existing data regarding the</p> <p>15 presence of any of these compounds in their</p> <p>16 talcum powder?</p> <p>17 A. Again, a complicated question.</p> <p>18 Asked who?</p> <p>19 Q. Did you ask to see any</p> <p>20 representative of Johnson & Johnson as to</p> <p>21 whether or not there was asbestos in their</p> <p>22 talcum powder?</p> <p>23 MS. MILLER: Objection.</p> <p>24 THE WITNESS: That sentence</p> <p>25 doesn't make sense.</p>

20 (Pages 74 to 77)

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<p style="text-align: right;">Page 78</p> <p>1 MS. MILLER: Yeah.</p> <p>2 THE WITNESS: I've never asked</p> <p>3 to see a representative of Johnson &</p> <p>4 Johnson.</p> <p>5 QUESTIONS BY MR. RESTAINO:</p> <p>6 Q. Did you ever ask to see any</p> <p>7 documentation that Johnson & Johnson may have</p> <p>8 regarding the presence of asbestos in their</p> <p>9 talcum powder?</p> <p>10 MS. MILLER: Objection.</p> <p>11 THE WITNESS: No.</p> <p>12 QUESTIONS BY MR. RESTAINO:</p> <p>13 Q. If there were asbestos in</p> <p>14 Johnson & Johnson's talcum powder, would that</p> <p>15 change any of your opinions that you had</p> <p>16 formulated within your expert report?</p> <p>17 A. My opinions are based on</p> <p>18 Johnson's baby powder, the use of Johnson's</p> <p>19 baby powder.</p> <p>20 Q. And the opinion you hold based</p> <p>21 on Johnson's baby powder, does that take into</p> <p>22 account the presence or absence of asbestos?</p> <p>23 MS. MILLER: Objection. Asked,</p> <p>24 answered and confusing.</p> <p>25 THE WITNESS: I assume nothing</p>	<p style="text-align: right;">Page 80</p> <p>1 on the pathomechanism of ovarian cancer?</p> <p>2 A. I don't believe pathomechanism</p> <p>3 is a word, but I'll give you a chance to</p> <p>4 rephrase it. Otherwise, I'll make my best</p> <p>5 attempt to infer what you were asking.</p> <p>6 Q. Has your research ever focused</p> <p>7 on the cause of ovarian cancer?</p> <p>8 A. How do you define "cause"?</p> <p>9 Q. As we go through today's</p> <p>10 deposition, I'd like to use your definition</p> <p>11 so you're most comfortable with it.</p> <p>12 How would you define a cause?</p> <p>13 MS. MILLER: Objection. Vague.</p> <p>14 THE WITNESS: It's impossible</p> <p>15 to answer.</p> <p>16 QUESTIONS BY MR. RESTAINO:</p> <p>17 Q. By whom?</p> <p>18 A. Me.</p> <p>19 Q. And why is that?</p> <p>20 A. Because cause has a multitude</p> <p>21 of meanings.</p> <p>22 Q. If I walk into this room at</p> <p>23 night and the light is off and it's dark and</p> <p>24 I flip the switch on, did I cause the light</p> <p>25 to go on?</p>
<p style="text-align: right;">Page 79</p> <p>1 other than what I read on the bottle</p> <p>2 about Johnson's baby powder.</p> <p>3 QUESTIONS BY MR. RESTAINO:</p> <p>4 Q. Do you know if Johnson &</p> <p>5 Johnson has any documentation of studies that</p> <p>6 they have performed showing the presence of</p> <p>7 asbestos in their talcum powder?</p> <p>8 A. I'm not aware of any studies</p> <p>9 that Johnson & Johnson has ever performed on</p> <p>10 anything.</p> <p>11 Q. Am I correct in understanding</p> <p>12 that as of today you are chair, department of</p> <p>13 human molecular genetics?</p> <p>14 A. At the Herbert Wertheim College</p> <p>15 of Medicine of Florida International</p> <p>16 University, yes, I'm a tenured professor and</p> <p>17 chair.</p> <p>18 Q. Are you also there an associate</p> <p>19 dean for basic research in graduate programs?</p> <p>20 A. Yes.</p> <p>21 Q. And are you professor of</p> <p>22 obstetrics and gynecology at the Herbert</p> <p>23 Wertheim College of Medicine?</p> <p>24 A. Yes.</p> <p>25 Q. Is your research ever focused</p>	<p style="text-align: right;">Page 81</p> <p>1 MS. MILLER: Objection.</p> <p>2 THE WITNESS: Again, that's a</p> <p>3 very complex question. One could</p> <p>4 argue that the electricity caused the</p> <p>5 light to go on, for example.</p> <p>6 QUESTIONS BY MR. RESTAINO:</p> <p>7 Q. One could argue that the wire</p> <p>8 has to be attached to the switch to the light</p> <p>9 bulb, correct?</p> <p>10 A. Correct.</p> <p>11 Q. One has to assume that the</p> <p>12 light bulb is a working light bulb, correct?</p> <p>13 A. Yes.</p> <p>14 Q. One has to assume that the law</p> <p>15 firm paid its electrical bill, correct?</p> <p>16 A. Correct.</p> <p>17 Q. Are you familiar with the</p> <p>18 multifactorial basis of disease?</p> <p>19 MS. MILLER: Objection.</p> <p>20 THE WITNESS: That is a, with</p> <p>21 all due respect, fabulously broad</p> <p>22 question.</p> <p>23 QUESTIONS BY MR. RESTAINO:</p> <p>24 Q. I think we'll revisit it.</p> <p>25 A. Which disease?</p>

21 (Pages 78 to 81)

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<p style="text-align: right;">Page 82</p> <p>1 Q. Ovarian cancer.</p> <p>2 A. So could you repeat the</p> <p>3 question with a more specific disease in</p> <p>4 mind, please?</p> <p>5 Q. Sure.</p> <p>6 Are you familiar with the</p> <p>7 multi -- what has been described as the</p> <p>8 multifactorial basis of ovarian cancer?</p> <p>9 A. I would have to say that I'm</p> <p>10 familiar in very general terms with the</p> <p>11 multifactorial basis of all human cancers,</p> <p>12 which would include ovarian.</p> <p>13 Q. Okay. Has your research ever</p> <p>14 focused on the epidemiology regarding chronic</p> <p>15 inflammation and the development of cancer?</p> <p>16 MS. MILLER: Objection.</p> <p>17 THE WITNESS: No.</p> <p>18 QUESTIONS BY MR. RESTAINO:</p> <p>19 Q. And --</p> <p>20 A. I'm sorry. And by research,</p> <p>21 I'm assuming you're referring to my own</p> <p>22 laboratory-based research?</p> <p>23 Q. Once again, I want to make sure</p> <p>24 we're using terms that you're most</p> <p>25 comfortable with.</p>	<p style="text-align: right;">Page 84</p> <p>1 MS. MILLER: Objection.</p> <p>2 THE WITNESS: I'm only prepared</p> <p>3 to answer that question in very</p> <p>4 general terms in the sense that my</p> <p>5 understanding of epidemiology is to</p> <p>6 study association of X and Y as</p> <p>7 opposed to causation. I distinguish</p> <p>8 association from causation.</p> <p>9 QUESTIONS BY MR. RESTAINO:</p> <p>10 Q. Does a randomized controlled</p> <p>11 trial establish causation in certain</p> <p>12 circumstances?</p> <p>13 MS. MILLER: Objection.</p> <p>14 THE WITNESS: It's a very vague</p> <p>15 and convoluted question that's</p> <p>16 impossible for me to answer.</p> <p>17 QUESTIONS BY MR. RESTAINO:</p> <p>18 Q. And is that because you're not</p> <p>19 an expert in epidemiology?</p> <p>20 MS. MILLER: Objection.</p> <p>21 THE WITNESS: I'm very familiar</p> <p>22 with the concept of clinical trials.</p> <p>23 I sat on the committee for</p> <p>24 experimental medicine for the</p> <p>25 gynecologic oncology group for</p>
<p style="text-align: right;">Page 83</p> <p>1 So do you do, for lack of a</p> <p>2 better description, bench-type of</p> <p>3 pharmacological research or genetic research?</p> <p>4 A. Certainly I don't do</p> <p>5 pharmacological bench research. I have for</p> <p>6 many years done molecular genetic and genetic</p> <p>7 research.</p> <p>8 I guess my reason for asking</p> <p>9 the question was because lawyers seem to use</p> <p>10 the term "research" referring to preparation</p> <p>11 for expert testimony in a deposition context.</p> <p>12 Q. In your professional setting,</p> <p>13 without lawyers being in the room, would your</p> <p>14 research also consist of analysis of the</p> <p>15 existing medical literature?</p> <p>16 MS. MILLER: Objection.</p> <p>17 THE WITNESS: I just find that,</p> <p>18 I'm sorry, a very weird question.</p> <p>19 I've never met a biomedical scientist</p> <p>20 who didn't read the literature.</p> <p>21 QUESTIONS BY MR. RESTAINO:</p> <p>22 Q. Do you agree or disagree that</p> <p>23 the epidemiologic evidence implicates chronic</p> <p>24 inflammation as a central mechanism in the</p> <p>25 pathogenesis of ovarian cancer?</p>	<p style="text-align: right;">Page 85</p> <p>1 17 years, and I can assure you that we</p> <p>2 rarely discuss epidemiology in the</p> <p>3 design of clinical trials.</p> <p>4 QUESTIONS BY MR. RESTAINO:</p> <p>5 Q. Okay. Do you agree or disagree</p> <p>6 that rapid cell division increases the</p> <p>7 possibility for DNA replication error?</p> <p>8 MS. MILLER: Objection.</p> <p>9 THE WITNESS: Again, a very</p> <p>10 vague question, but I'll offer an</p> <p>11 opinion. DNA replication error is</p> <p>12 impossible absent cell division.</p> <p>13 QUESTIONS BY MR. RESTAINO:</p> <p>14 Q. So would you agree that the</p> <p>15 possibility for DNA replication error is</p> <p>16 increased with rapid cell division?</p> <p>17 A. I'll give you the same answer:</p> <p>18 Cell division is required for errors in DNA</p> <p>19 replication.</p> <p>20 Q. Okay. Would you agree or</p> <p>21 disagree that rapid cell division increases</p> <p>22 the possibility of ineffective DNA repair?</p> <p>23 A. It's the same question asked in</p> <p>24 a different fashion, and I've answered it</p> <p>25 twice, with all due respect.</p>

22 (Pages 82 to 85)

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<p style="text-align: right;">Page 86</p> <p>1 MS. MILLER: With all due 2 respect, you didn't give me a chance 3 to object that it was asked and 4 answered. 5 THE WITNESS: So noted. 6 QUESTIONS BY MR. RESTAINO: 7 Q. Do you agree or disagree that 8 rapid cell division increases the possibility 9 of subsequent mutation? 10 MS. MILLER: Objection. 11 THE WITNESS: Same question. 12 Answered. 13 QUESTIONS BY MR. RESTAINO: 14 Q. Okay. Now, the expert report 15 that I believe you still have in front of 16 you, did you write the entire expert report 17 yourself? 18 A. Yes. 19 Q. Did you do the -- any research 20 that you needed to do for your expert report 21 by yourself? 22 A. Yes. 23 Q. In your general scientific 24 publications, do you utilize research 25 assistants, post-grad fellows, individuals</p>	<p style="text-align: right;">Page 88</p> <p>1 A. I can only accurately answer 2 that question by asking you a question. 3 Q. Yes, sir. 4 A. When you say "medical 5 literature," do you mean medical and 6 scientific literature? 7 Q. Yes, please. Let me correct 8 that. 9 And going forward for today, 10 would it be more comfortable for you to be -- 11 to refer to it as the scientific literature, 12 to encompass both medical and scientific, or 13 would you like them bifurcated? 14 What would be most comfortable 15 for you? 16 A. The term I prefer is biomedical 17 literature. 18 Q. Biomedical? 19 A. Yes. 20 Q. Did you do the biomedical 21 research yourself prior to writing your 22 expert report? 23 MS. MILLER: Objection. 24 THE WITNESS: Yes. 25</p>
<p style="text-align: right;">Page 87</p> <p>1 like that? 2 A. I'm sorry, please repeat the 3 question. 4 Q. Yes. 5 In your professional life, if 6 you're going to be writing a review article 7 or an original piece, do you utilize post-doc 8 fellows, residents, research fellows, any 9 individuals like that that are still in 10 training to assist you in your research? 11 A. Yes. 12 Q. And did any of those type of 13 individuals assist you with the research 14 necessary to write your expert report today? 15 A. No. 16 Q. Okay. Did you review germane 17 medical literature for -- prior to writing 18 your expert report? 19 A. Well, I don't think I reviewed 20 non-germane medical or scientific literature, 21 so I suppose the default answer is yes. 22 Q. Okay. Well, what methodology 23 did you employ in order to conduct your 24 research of the medical literature prior to 25 writing your expert report?</p>	<p style="text-align: right;">Page 89</p> <p>1 QUESTIONS BY MR. RESTAINO: 2 Q. And what was the methodology 3 that you employed? 4 A. Well, other than reading expert 5 reports and deposition transcripts, which I 6 think we can all agree were provided for me, 7 I think I utilized a methodology that most 8 would agree is standard, which would involve 9 PubMed searches and perhaps to a lesser 10 extent Google searches. 11 Q. In conducting your PubMed and 12 perhaps to a lesser extent Google searches, 13 did you utilize keywords to find the 14 particular articles you may have been looking 15 for? 16 A. I'm not aware of any other way 17 to do a search without keywords. 18 Q. And as you sit here today, can 19 you share with us some of the keywords you 20 utilized? 21 A. "Ovarian," "cancer," "talc," 22 "talcum powder." I honestly don't remember 23 any other words. 24 Q. How about "inflammation"? 25 A. So I'm aware of having come</p>

23 (Pages 86 to 89)

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<p style="text-align: right;">Page 90</p> <p>1 across papers having to do with, for example, 2 inflammation insofar as the keywords that I 3 recall using led me to papers that had 4 concepts embedded in them as perhaps 5 citations, which would lead me to look up a 6 citation typically with an author's name, a 7 page number, a journal, for example. 8 I don't recall performing a 9 literature search using the term 10 "inflammation" specifically. 11 Q. Forgive me for paraphrasing an 12 earlier answer you may have given, but my 13 understanding was that your understanding for 14 your purpose of being here today was to 15 discuss Dr. Saed's expert report and his 16 experiment and the biological plausibility as 17 put forth by the plaintiff attorneys. 18 Am I wrong with that? 19 MS. MILLER: Objection. 20 THE WITNESS: It's my 21 understanding that my purpose for 22 being here today is to discuss 23 Dr. Saed's work, his published work, 24 his deposition transcript, his expert 25 report specifically, and in a more</p>	<p style="text-align: right;">Page 92</p> <p>1 with the role of inflammation? 2 A. He -- I'm sorry, repeat the 3 question, please. 4 Q. Did Dr. Saed's experiment 5 pertaining to biological plausibility involve 6 the role of inflammation? 7 A. He claims that it did. 8 Q. And I believe you testified 9 earlier that you either read or skimmed the 10 study that was authored by Dr. Shih and 11 attached to his expert report; is that 12 correct? 13 A. I took a very quick look at it. 14 Q. Do you know -- I'm sorry, 15 forgive me. 16 Were you finished? 17 A. Yes. 18 Q. Do you know if a component of 19 that study had to do with the 20 histopathological analysis of the presence or 21 absence of inflammation? 22 A. I honestly can't recall. 23 Q. Did you write in its entirety 24 your expert report by yourself? 25 A. I'm pretty sure you asked</p>
<p style="text-align: right;">Page 91</p> <p>1 general sense biologic plausibility. 2 QUESTIONS BY MR. RESTAINO: 3 Q. Okay. And you understand that 4 a key component of the biological 5 plausibility argument put forth by the 6 plaintiff experts involves the role of 7 chronic inflammation in the development of 8 ovarian cancer? 9 MS. MILLER: Objection. 10 THE WITNESS: I'm sorry, could 11 you repeat the question? 12 QUESTIONS BY MR. RESTAINO: 13 Q. You understand that a key 14 component of the biological plausibility 15 argument put forth by the plaintiff experts 16 involves the role of chronic inflammation in 17 the development of ovarian cancer? 18 MS. MILLER: Objection. 19 THE WITNESS: I can certainly 20 say that I'm most familiar with 21 Dr. Saed's work addressing hypotheses 22 related to biologic plausibility. 23 QUESTIONS BY MR. RESTAINO: 24 Q. Did Dr. Saed's work pertaining 25 to the biological plausibility have to deal</p>	<p style="text-align: right;">Page 93</p> <p>1 before, and I said yes. 2 Q. Okay. Are the words and the 3 language in your report your choice of 4 language? 5 A. It's the same question, but, 6 yes. 7 Q. Are all your opinions that you 8 will be offering regarding the role of 9 Dr. Saed's report and study and the role of 10 biological plausibility contained within your 11 expert report? 12 A. I'm sorry, I thought you were 13 heading somewhere else with the prelude. 14 Could you repeat the question, 15 please? 16 Q. Are all the opinions you will 17 be offering regarding the role of Dr. Saed's 18 report and study and the role of biological 19 plausibility contained within your expert 20 report? 21 A. I'm sure my expert report could 22 have been longer, so that's really a 23 difficult question to answer. 24 Q. As you sit here today, do you 25 have any other opinions that you have not put</p>

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<p style="text-align: right;">Page 94</p> <p>1 into your expert report regarding Dr. Saed --</p> <p>2 A. That's just -- I'm sorry for</p> <p>3 laughing. It's a serious -- you're a serious</p> <p>4 man. I'm a serious man. It's a serious</p> <p>5 issue.</p> <p>6 But I just find it an</p> <p>7 incredibly difficult question to answer, I'm</p> <p>8 sorry.</p> <p>9 Q. I'm going to try to make it as</p> <p>10 easy as possible.</p> <p>11 Other than that which you've</p> <p>12 written in your expert report, since the date</p> <p>13 of signing your report, have you established</p> <p>14 any other opinion regarding Dr. Saed's study,</p> <p>15 Dr. Saed's expert report or the biological</p> <p>16 plausibility regarding talcum powder and</p> <p>17 ovarian cancer?</p> <p>18 MS. MILLER: Objection.</p> <p>19 THE WITNESS: Well, I've read</p> <p>20 Dr. Saed's subsequent published paper</p> <p>21 in Reproductive Sciences, which</p> <p>22 happened after I prepared my expert</p> <p>23 report, and I've formed some opinions</p> <p>24 about the content of that paper.</p> <p>25</p>	<p style="text-align: right;">Page 96</p> <p>1 other expert opinion you've developed since</p> <p>2 you've signed your expert report that you</p> <p>3 would be offering. And we have a right to</p> <p>4 know what that expert opinion is.</p> <p>5 A. I'll do my best to answer</p> <p>6 whichever questions you choose to ask me. I</p> <p>7 think about this a lot.</p> <p>8 Q. Have --</p> <p>9 A. In the middle of the night, for</p> <p>10 example.</p> <p>11 I can't honestly say that I'm</p> <p>12 forming expert opinions, but, you know, it's</p> <p>13 consumed a lot of my free time over the past</p> <p>14 several months.</p> <p>15 Q. As you've thought about this</p> <p>16 since you've signed and submitted your expert</p> <p>17 report, have you developed any opinions that</p> <p>18 are in disagreement with that which you have</p> <p>19 listed in your expert report?</p> <p>20 A. No.</p> <p>21 Q. Do you consider yourself an</p> <p>22 expert in the carcinogenicity of ovarian</p> <p>23 cancer?</p> <p>24 MS. MILLER: Objection.</p> <p>25 THE WITNESS: And so I suppose</p>
<p style="text-align: right;">Page 95</p> <p>1 QUESTIONS BY MR. RESTAINO:</p> <p>2 Q. Okay. Are those opinions</p> <p>3 listed in your expert report?</p> <p>4 MS. MILLER: Objection.</p> <p>5 THE WITNESS: You obviously</p> <p>6 misunderstood my answer.</p> <p>7 QUESTIONS BY MR. RESTAINO:</p> <p>8 Q. Well, you said -- what you said</p> <p>9 was, "Well, I read Dr. Saed's subsequent</p> <p>10 published paper in Reproductive Sciences,</p> <p>11 which happened after I prepared my expert</p> <p>12 report."</p> <p>13 Was that, after you prepared</p> <p>14 it, also after you finalized it and signed</p> <p>15 it?</p> <p>16 MS. MILLER: As you know, it</p> <p>17 wasn't published until after</p> <p>18 February 25, so I don't really know</p> <p>19 where you're headed here.</p> <p>20 MR. RESTAINO: So I</p> <p>21 misunderstood, and I'll strike the</p> <p>22 question.</p> <p>23 QUESTIONS BY MR. RESTAINO:</p> <p>24 Q. Doctor, I'm just trying to</p> <p>25 learn if there's anything else that -- any</p>	<p style="text-align: right;">Page 97</p> <p>1 when I ask you, how do you define</p> <p>2 carcinogenicity, you're going to ask</p> <p>3 me how do I define carcinogenicity?</p> <p>4 QUESTIONS BY MR. RESTAINO:</p> <p>5 Q. I'm going to fool you this</p> <p>6 time.</p> <p>7 How about carcinogenicity is</p> <p>8 the ability or tendency of an agent to induce</p> <p>9 tumors, benign or malignant, increase their</p> <p>10 incidence or malignancy, or shorten the time</p> <p>11 of tumor occurrence when it is inhaled,</p> <p>12 ingested, dermally applied or injected, does</p> <p>13 that sound like a reasonable definition?</p> <p>14 A. That's the Google dictionary</p> <p>15 definition.</p> <p>16 Q. I disagree, but it's a</p> <p>17 definition.</p> <p>18 A. It's certainly a definition.</p> <p>19 Q. Is it a reasonable definition?</p> <p>20 A. It's a reasonable definition.</p> <p>21 Q. Okay. Are you familiar with</p> <p>22 what has been described as the hallmarks of</p> <p>23 carcinogenicity as published by Hanahan and</p> <p>24 Weinberg in 1990?</p> <p>25 A. No.</p>

25 (Pages 94 to 97)

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<p style="text-align: right;">Page 98</p> <p>1 You got the title wrong, and</p> <p>2 you got the date wrong.</p> <p>3 Q. How so?</p> <p>4 A. They've published two versions,</p> <p>5 one in 2000 and one in 2011, and</p> <p>6 carcinogenicity is not in the title.</p> <p>7 Q. I wasn't actually asking for</p> <p>8 the title of the paper, but are you -- you're</p> <p>9 obviously then familiar with Hallmarks of</p> <p>10 Cancer as published in 1990?</p> <p>11 A. No.</p> <p>12 Q. Is there a different title?</p> <p>13 A. No, there's a different date.</p> <p>14 Q. 2000. I'm sorry, in 2000.</p> <p>15 A. It's okay.</p> <p>16 I have very little memory of</p> <p>17 the original 2000 paper. I've certainly read</p> <p>18 the paper published -- the update, the</p> <p>19 version of the paper published in 2011.</p> <p>20 Q. As you sit here today, can you</p> <p>21 share with us any of the recognized hallmarks</p> <p>22 of cancer?</p> <p>23 MS. MILLER: Objection.</p> <p>24 THE WITNESS: I'd be happy to</p> <p>25 go over them with you if you could</p>	<p style="text-align: right;">Page 100</p> <p>1 attorneys in a previous deposition</p> <p>2 transcript, but I'll let you recapitulate the</p> <p>3 number for me, if that's what you're</p> <p>4 interested in doing.</p> <p>5 Q. I'll come back.</p> <p>6 A. Okay.</p> <p>7 Q. We've talked a little bit about</p> <p>8 a risk factor, correct?</p> <p>9 A. I seem to recall the question</p> <p>10 as to how do I define a risk factor, yeah.</p> <p>11 Q. Do you agree that there are</p> <p>12 certain risk factors that are associated with</p> <p>13 the development of ovarian cancer?</p> <p>14 A. Yes.</p> <p>15 Q. Would you agree that for a risk</p> <p>16 factor to be a true risk factor, it must be</p> <p>17 biologically plausible?</p> <p>18 A. "True" is an overly subjective</p> <p>19 and impossible to interpret term from a</p> <p>20 scientist's -- from a scientific standpoint.</p> <p>21 Q. Would you agree that for a risk</p> <p>22 factor to be an accurate risk factor, it must</p> <p>23 be biologically plausible?</p> <p>24 A. Same answer.</p> <p>25 Q. Would you agree that a risk</p>
<p style="text-align: right;">Page 99</p> <p>1 produce a copy of the paper. It's a</p> <p>2 extraordinarily comprehensive overview</p> <p>3 of cancer generally that's typically</p> <p>4 used to inform nonexperts in the</p> <p>5 field.</p> <p>6 QUESTIONS BY MR. RESTAINO:</p> <p>7 Q. What is the objective basis for</p> <p>8 your opinion that it is typically used to</p> <p>9 inform nonexperts in the field?</p> <p>10 A. Experts in the field of cancer</p> <p>11 generally are familiar with the concepts</p> <p>12 articulated by the authors.</p> <p>13 I, for example, use Figure 1</p> <p>14 when I'm giving lectures to lay people,</p> <p>15 general practitioners, medical students, for</p> <p>16 example.</p> <p>17 Q. And how about other</p> <p>18 researchers? Do you know how they use the</p> <p>19 publication?</p> <p>20 A. I certainly can't speak to how</p> <p>21 other researchers use any publication.</p> <p>22 Q. Do you know how often that</p> <p>23 paper has been cited by medical researchers?</p> <p>24 A. I could try to recall the</p> <p>25 number that was offered by plaintiffs'</p>	<p style="text-align: right;">Page 101</p> <p>1 factor for the development of a disease such</p> <p>2 as ovarian cancer must have a biologically</p> <p>3 plausible basis in order to be an accurate</p> <p>4 risk?</p> <p>5 A. Reusing the same words, so I</p> <p>6 would have to give you the same answer.</p> <p>7 Q. I'm just trying to make it</p> <p>8 easier for you. Let me try using an example.</p> <p>9 Would you agree that aside from</p> <p>10 gender, which is a given, that a woman over</p> <p>11 age 45 is at increased risk for developing</p> <p>12 ovarian cancer than a woman in her 20s?</p> <p>13 MS. MILLER: Objection.</p> <p>14 THE WITNESS: A great majority</p> <p>15 of human cancers, other than those</p> <p>16 that occur in kids, which are very</p> <p>17 limited in scope, are diseases of</p> <p>18 aging, generally speaking. So age is,</p> <p>19 in and of itself, a risk factor for</p> <p>20 virtually all cancers that occur in</p> <p>21 adults.</p> <p>22 QUESTIONS BY MR. RESTAINO:</p> <p>23 Q. Is age a biologically plausible</p> <p>24 risk factor?</p> <p>25 MS. MILLER: Objection.</p>

26 (Pages 98 to 101)

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<p style="text-align: right;">Page 102</p> <p>1 THE WITNESS: Yes.</p> <p>2 QUESTIONS BY MR. RESTAINO:</p> <p>3 Q. How about a woman of Jewish</p> <p>4 ethnicity? Does a woman over the age of 55</p> <p>5 who is of Jewish ethnicity have an increased</p> <p>6 risk for the development of ovarian cancer</p> <p>7 than a non-Jewish woman who is in her 20s?</p> <p>8 MS. MILLER: Objection.</p> <p>9 THE WITNESS: Ashkenazi</p> <p>10 Jewish --</p> <p>11 QUESTIONS BY MR. RESTAINO:</p> <p>12 Q. If you like.</p> <p>13 A. -- question mark?</p> <p>14 Q. Yes.</p> <p>15 MS. MILLER: Still objection.</p> <p>16 THE WITNESS: You've conflated</p> <p>17 two questions into one, I'm sorry.</p> <p>18 You've -- you've asked about</p> <p>19 Jewish women of a certain age and</p> <p>20 non-Jewish women of a certain age.</p> <p>21 Could we break -- could we</p> <p>22 parse out the question?</p> <p>23 QUESTIONS BY MR. RESTAINO:</p> <p>24 Q. Are women of Jewish ethnicity</p> <p>25 at a higher risk of developing ovarian cancer</p>	<p style="text-align: right;">Page 104</p> <p>1 A. Thank you.</p> <p>2 Q. -- in 2013 do you recall</p> <p>3 publishing "Metastasis Dynamics for a</p> <p>4 Non-Small-Cell Lung Cancer: Effect of</p> <p>5 Patient and Tumor-Related Factors"?</p> <p>6 A. I'm sorry, I -- no.</p> <p>7 Q. Okay. Fair enough.</p> <p>8 Would you agree that some of</p> <p>9 the pathological factors that are associated</p> <p>10 with reoccurrence of cancer, specifically</p> <p>11 lung cancer, would be, A, size of the primary</p> <p>12 tumor?</p> <p>13 A. I'm not an expert in lung</p> <p>14 cancer.</p> <p>15 Q. Would it be the same answer</p> <p>16 for -- if there was lymph node involvement?</p> <p>17 MS. MILLER: Objection.</p> <p>18 Same answer to what? Could you</p> <p>19 just make that question clearer?</p> <p>20 MR. RESTAINO: Sure. Sure.</p> <p>21 QUESTIONS BY MR. RESTAINO:</p> <p>22 Q. Would you agree that one of the</p> <p>23 pathological factors associated with a higher</p> <p>24 risk of reoccurrence in any cancer, but let's</p> <p>25 limit it to non-small cell lung cancer, would</p>
<p style="text-align: right;">Page 103</p> <p>1 than women of non-Jewish ethnicity?</p> <p>2 MS. MILLER: Objection.</p> <p>3 THE WITNESS: Ashkenazi Jews,</p> <p>4 generally speaking, carry mutations in</p> <p>5 the BRCA1 and 2 genes at a much higher</p> <p>6 frequency than individuals in the</p> <p>7 non-Ashkenazi Jewish population.</p> <p>8 MS. MILLER: Stop reminding me.</p> <p>9 THE WITNESS: And I would</p> <p>10 remind you that men do as well, of the</p> <p>11 same ethnicity.</p> <p>12 QUESTIONS BY MR. RESTAINO:</p> <p>13 Q. But men are not at a risk for</p> <p>14 ovarian cancer, correct?</p> <p>15 A. No, but they're certainly at</p> <p>16 risk for male breast cancer, which is</p> <p>17 associated with BRCA2 in particular.</p> <p>18 Q. BRCA1 and 2, are they</p> <p>19 biologically plausible risk factors for the</p> <p>20 development of ovarian cancer in women?</p> <p>21 A. Yes.</p> <p>22 Q. Doctor, you've written also on</p> <p>23 the risk factors of carcinogenicity. And</p> <p>24 without playing any word games or trying to</p> <p>25 ask you when and where --</p>	<p style="text-align: right;">Page 105</p> <p>1 include lymph node involvement?</p> <p>2 A. I would agree that the risk of</p> <p>3 recurrence of virtually all human cancers is</p> <p>4 increased with higher stage, and lymph node</p> <p>5 involvement is typically associated with a</p> <p>6 higher pathologic or -- and/or clinical</p> <p>7 stage.</p> <p>8 Q. Is that a biologically</p> <p>9 plausible risk factor for reoccurrence?</p> <p>10 A. Could you ask the complete</p> <p>11 question, please?</p> <p>12 Q. Would the lymph node</p> <p>13 involvement of any cancer be associated with</p> <p>14 a biologically plausible increased risk of</p> <p>15 reoccurrence of that cancer?</p> <p>16 A. Yes.</p> <p>17 Q. And as a physician -- excuse</p> <p>18 me. As scientist of your gravitas, would you</p> <p>19 agree that you would not publish the risk</p> <p>20 factors of any cancer, whether it be the</p> <p>21 origin of the cancer or the reoccurrence, if</p> <p>22 the risk factor did not have a biologically</p> <p>23 plausible basis; is that a fair enough</p> <p>24 statement?</p> <p>25 MS. MILLER: Objection.</p>

27 (Pages 102 to 105)

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<p style="text-align: right;">Page 106</p> <p>1 THE WITNESS: Well, I hope it's</p> <p>2 a question, first of all.</p> <p>3 And could you please repeat it?</p> <p>4 QUESTIONS BY MR. RESTAINO:</p> <p>5 Q. Yes.</p> <p>6 Doctor, as a scientist with</p> <p>7 your gravitas --</p> <p>8 A. Thank you.</p> <p>9 Q. -- would you agree you would</p> <p>10 not publish in the peer-reviewed medical --</p> <p>11 biomedical literature on the risk factor of</p> <p>12 any cancer, be it may -- be as it may the</p> <p>13 origin of that cancer or the reoccurrence of</p> <p>14 that cancer unless the risk factors had a</p> <p>15 biologically plausible basis?</p> <p>16 MS. MILLER: Objection.</p> <p>17 THE WITNESS: I would say that</p> <p>18 generally speaking, biological</p> <p>19 plausibility in the context of cancer</p> <p>20 generally is more important when the</p> <p>21 level of risk associated with the</p> <p>22 hypothesized risk factor is very low.</p> <p>23 So in other words, to give you</p> <p>24 an example, I would suggest that</p> <p>25 biological plausibility linking</p>	<p style="text-align: right;">Page 108</p> <p>1 It's not a memory test, as I</p> <p>2 recall.</p> <p>3 Q. No, it isn't, and I'm not going</p> <p>4 to test your memory in areas there.</p> <p>5 Have you published in the</p> <p>6 biomedical literature on the role of the</p> <p>7 BRCA1 and BRCA2 mutations and their role with</p> <p>8 breast cancer?</p> <p>9 A. Yes.</p> <p>10 Q. Have you published with those</p> <p>11 mutations and their role in ovarian cancer?</p> <p>12 A. Yes.</p> <p>13 Q. Have you published on the role</p> <p>14 of Jewish ethnicity and the development of</p> <p>15 ovarian cancer?</p> <p>16 A. Jewish ethnicity, per se, no.</p> <p>17 Q. And how about any specific type</p> <p>18 of form of Jewish ethnicity?</p> <p>19 A. I'm not getting at Ashkenazi</p> <p>20 versus Sephardic. I'm getting at ethnicity,</p> <p>21 per se, as opposed to the prevalence of BRCA</p> <p>22 mutations in the Ashkenazi.</p> <p>23 Q. Regarding the development of</p> <p>24 ovarian cancer, do you recognize family</p> <p>25 history as a biologically plausible risk</p>
<p style="text-align: right;">Page 107</p> <p>1 cigarette smoking to lung cancer is</p> <p>2 less important because of the enormous</p> <p>3 magnitude of the association,</p> <p>4 consistent and large over decades of</p> <p>5 study.</p> <p>6 QUESTIONS BY MR. RESTAINO:</p> <p>7 Q. Using cigarette smoking --</p> <p>8 A. As an example. I'm sorry to</p> <p>9 interrupt.</p> <p>10 Q. I'm sorry.</p> <p>11 Using cigarette smoking also an</p> <p>12 as example then, cigarette smoking is also</p> <p>13 associated with cardiovascular disease; would</p> <p>14 you agree?</p> <p>15 A. Yes.</p> <p>16 Q. Would you also agree that the</p> <p>17 risk ratio associated with cigarette smoking</p> <p>18 and cardiovascular disease is far less than</p> <p>19 the risk ratio of cigarette smoking and lung</p> <p>20 cancer?</p> <p>21 A. I can't comment on the</p> <p>22 relative -- I can't comment with authority on</p> <p>23 the magnitude of the risk factors for</p> <p>24 cardiovascular disease compared to lung</p> <p>25 cancer associated with cigarette smoking.</p>	<p style="text-align: right;">Page 109</p> <p>1 factor?</p> <p>2 MS. MILLER: Objection.</p> <p>3 THE WITNESS: Well, you're</p> <p>4 using the word "biological</p> <p>5 plausibility" with "risk factor,"</p> <p>6 which is, I have to say, a strange</p> <p>7 concept for me.</p> <p>8 I'm familiar with the concept</p> <p>9 of getting from association in an</p> <p>10 epidemiologic context to causality in</p> <p>11 a biological context using biological</p> <p>12 plausibility as a tool when and, in</p> <p>13 context, where it may be most</p> <p>14 necessary.</p> <p>15 QUESTIONS BY MR. RESTAINO:</p> <p>16 Q. Okay. And in using the term as</p> <p>17 you're most familiar with it, would you</p> <p>18 publish on risk factors for any cancer if, in</p> <p>19 your opinion, that risk factor was not</p> <p>20 biologically plausible?</p> <p>21 MS. MILLER: Objection.</p> <p>22 THE WITNESS: It's just a very</p> <p>23 vague question. Hard to answer.</p> <p>24 If you'd like to refer me to</p> <p>25 one of my specific publications, I'd</p>

28 (Pages 106 to 109)

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<p style="text-align: right;">Page 110</p> <p>1 be happy to address the rationale</p> <p>2 underlying my reasons for publishing</p> <p>3 the data contained in that</p> <p>4 publication.</p> <p>5 QUESTIONS BY MR. RESTAINO:</p> <p>6 Q. Well, I mentioned previously</p> <p>7 the "Metastasis Dynamics for Non-Small-Cell</p> <p>8 Lung Cancer: Effect of Patient and</p> <p>9 Tumor-Related Factors," but as you sit here</p> <p>10 today, you do not recall that, correct?</p> <p>11 A. All I heard, with all due</p> <p>12 respect, sir, is a jumble of words. It</p> <p>13 doesn't even sound like the title of a paper.</p> <p>14 But to the extent that you're</p> <p>15 probably reading from my CV, I don't recall</p> <p>16 the paper.</p> <p>17 Q. Okay.</p> <p>18 MS. MILLER: Is this a good</p> <p>19 time for a break?</p> <p>20 MR. RESTAINO: Sure.</p> <p>21 MS. MILLER: Great.</p> <p>22 VIDEOGRAPHER: Off the record</p> <p>23 at 11:16 a.m.</p> <p>24 (Off the record at 11:16 a.m.)</p> <p>25 VIDEOGRAPHER: We are back on</p>	<p style="text-align: right;">Page 112</p> <p>1 which talc causes the transformation of a</p> <p>2 normal cell into a cell that ultimately</p> <p>3 manifests as the multiple different tumor</p> <p>4 types that we collectively refer to as</p> <p>5 epithelial ovarian carcinoma.</p> <p>6 Q. And have you ever been asked in</p> <p>7 your professional career to review another</p> <p>8 expert's expert report?</p> <p>9 A. Before this litigation?</p> <p>10 Q. Yes, sir.</p> <p>11 A. Yes. Again, I would remind you</p> <p>12 of the one other case, other than the</p> <p>13 administrative issues in Miami, in the late</p> <p>14 '90s, early 2000s, which was litigation</p> <p>15 involving -- well, to answer your question,</p> <p>16 yes, several decades ago.</p> <p>17 Q. And also at that time, were you</p> <p>18 asked to review any underlying notebook or</p> <p>19 laboratory documentation that might have been</p> <p>20 used as the basis for any opinions in that</p> <p>21 expert report?</p> <p>22 A. No.</p> <p>23 Q. Have you ever, in your</p> <p>24 professional career, been asked to review the</p> <p>25 notebook and underlying laboratory documents</p>
<p style="text-align: right;">Page 111</p> <p>1 the record at 11:31 a.m.</p> <p>2 QUESTIONS BY MR. RESTAINO:</p> <p>3 Q. Welcome back, Dr. Boyd.</p> <p>4 Dr. Boyd, do you intend to</p> <p>5 offer an opinion as to whether or not talc</p> <p>6 powder particles can migrate to the ovaries?</p> <p>7 A. No.</p> <p>8 Q. Now, with your expert report,</p> <p>9 if you would turn to page 2. And by that I</p> <p>10 mean the numbered page 2. All right?</p> <p>11 You have a Section 2, Scope of</p> <p>12 Report. And the first sentence there: "I</p> <p>13 was asked to opine on Dr. Ghassan Saed's</p> <p>14 expert report based on my experience as a</p> <p>15 molecular biologist in cancer research, and</p> <p>16 in particular, whether this research supports</p> <p>17 the biological plausibility of the</p> <p>18 plaintiff's theory that perineal talc use</p> <p>19 causes ovarian cancer."</p> <p>20 And, Doctor, did I read that</p> <p>21 correctly?</p> <p>22 A. You correctly read those words.</p> <p>23 Q. Now, as you wrote them there,</p> <p>24 how are you using biological plausibility?</p> <p>25 A. The biological process through</p>	<p style="text-align: right;">Page 113</p> <p>1 from an individual's experiments?</p> <p>2 A. Well, that's a pretty broad</p> <p>3 question. I have been the principal</p> <p>4 investigator in many laboratories, and I</p> <p>5 reviewed many laboratory notebooks. I have</p> <p>6 created many laboratory notebooks personally</p> <p>7 in the earlier stages of my career.</p> <p>8 And to reiterate, in the more</p> <p>9 senior stages of my career as a principal</p> <p>10 investigator heading up a laboratory, larger</p> <p>11 or smaller as it might be, I have reviewed a</p> <p>12 multitude of laboratory notebooks, yes.</p> <p>13 Q. Have you ever had -- have you</p> <p>14 ever been asked to review the laboratory</p> <p>15 notebook for any researchers not associated</p> <p>16 with your laboratory?</p> <p>17 A. Yes.</p> <p>18 Q. And under what circumstances?</p> <p>19 A. Alleged scientific fraud at an</p> <p>20 institution where I was in one case the chief</p> <p>21 scientific officer and in another case the</p> <p>22 chair of the department in which the alleged</p> <p>23 fraud took place.</p> <p>24 Q. If you would turn now to --</p> <p>25 stay on page 2 of your expert report. The</p>

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<p>1 top paragraph, third line down, first full 2 sentence you write, "My current research 3 interests." 4 Do you see that, sir? 5 A. Yes. 6 Q. "My current research interests 7 include the histogenesis, open paren, cell of 8 origin, close paren, of ovarian cancer, the 9 comprehensive genomic characterization of 10 ovarian cancer stem cells, and the genomic 11 basis of diethylstilbestrol, open paren, DES, 12 close paren, hyphen, induced carcinogenesis 13 of the cervix and vagina of women exposed to 14 DES in utero." 15 Did I read that correctly? 16 A. You read it perfectly. 17 Q. Okay. Is DES a form of 18 synthetic estrogen? 19 A. DES is indeed a synthetic 20 estrogen. 21 Q. And does the prenatal exposure 22 to DES cause subsequent development of clear 23 cell adenocarcinoma in the lower reproductive 24 tract of some daughters of women who have 25 taken the drug?</p>	<p>1 as opposed to in animals or lower 2 organisms or cells and so forth, in 3 humans we tend to make these 4 conclusions based on the strengths of 5 the association. 6 And in this particular case, 7 clear cell carcinomas of the vagina 8 and cervix are, generally speaking, 9 extremely rare tumors. Furthermore, 10 in young women, for example, 11 teenagers, women in their 20s, they're 12 virtually unheard of. 13 And so in 1971, more or less, 14 when Dr. Arthur Herbst at the 15 University of Chicago published a 16 paper in the New England Journal 17 describing a cluster of cases of clear 18 cell adenocarcinoma of the 19 cervicovaginal region in women exposed 20 to DES in utero, this was such a rare 21 confluence of an environmental, if you 22 will, or biological exposure to a 23 xenobiotic and the development of an 24 otherwise virtually unheard of cancer 25 in terms of the cancer and the age of</p>
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<p>1 A. It has been associated with the 2 development of aforementioned tumors in the 3 context that you've described, yes. 4 Q. My question was: "Does the 5 prenatal exposure to DES cause subsequent 6 development of clear cell adenocarcinoma?" 7 And your answer involved the 8 word "association." 9 A. Yes. 10 Q. So let me reask my question, if 11 I may. 12 Does the prenatal exposure to 13 DES cause subsequent development of clear 14 cell adenocarcinoma in the lower reproductive 15 tract of some daughters of women who have 16 taken the drug? 17 MS. MILLER: Objection. 18 THE WITNESS: In humans, for a 19 given human patient, it should be 20 rather self-evident that it's 21 virtually impossible to ascribe -- or 22 attribute, I'm sorry, the development 23 of a particular cancer to a particular 24 exposure in a given individual. 25 So we look typically, in humans</p>	<p>1 the women developing it, that the 2 strength of the association was, in 3 the minds of many at the time, 4 sufficient to attribute causality 5 between the in utero exposure to DES 6 and the development of the clear cell 7 cancer in the young women. 8 I hope that was a cogent answer 9 to your question. 10 QUESTIONS BY MR. RESTAINO: 11 Q. Yes. 12 Do you rely heavily upon 13 strength of association to determine a 14 causation? 15 MS. MILLER: Objection. 16 THE WITNESS: I'm sorry, I was 17 distracted by the -- 18 MS. MILLER: Yeah, is there -- 19 is that on there on purpose? 20 THE WITNESS: I just keep 21 looking at my CV and wondering -- 22 MS. MILLER: With the little 23 green sticky on it? 24 MR. RESTAINO: No. 25 THE WITNESS: I guess it's</p>

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<p style="text-align: right;">Page 118</p> <p>1 the --</p> <p>2 MR. RESTAINO: We can probably</p> <p>3 turn this off.</p> <p>4 THE WITNESS: There's a camera</p> <p>5 there or something.</p> <p>6 MS. MILLER: Well, why don't</p> <p>7 you turn that off, because it is</p> <p>8 distracting.</p> <p>9 THE WITNESS: I apologize.</p> <p>10 MR. RESTAINO: No, there's no</p> <p>11 apology necessary.</p> <p>12 THE WITNESS: Yeah.</p> <p>13 And could you repeat the</p> <p>14 question, please?</p> <p>15 QUESTIONS BY MR. RESTAINO:</p> <p>16 Q. Well, yes.</p> <p>17 My question, you know, was:</p> <p>18 Does the prenatal exposure to DES cause the</p> <p>19 subsequent development of clear cell</p> <p>20 adenocarcinoma in the lower reproductive</p> <p>21 tract in the daughters of women who have</p> <p>22 taken the drug?</p> <p>23 A. Well, again, I respectfully</p> <p>24 submit that I've answered the question. I'll</p> <p>25 answer it again.</p>	<p style="text-align: right;">Page 120</p> <p>1 page 13 of that document.</p> <p>2 A. All right. I'm sorry, let</p> <p>3 me -- could I just look at, for a moment, the</p> <p>4 document in its entirety?</p> <p>5 And which page, please?</p> <p>6 Q. Page 13.</p> <p>7 Actually, let's look on page 15</p> <p>8 of the document. There's a heading there,</p> <p>9 "Chemicals and Hormonal Cancers."</p> <p>10 Do you see that, sir?</p> <p>11 A. Uh-huh.</p> <p>12 Q. Now, in the middle of that</p> <p>13 paragraph, the big paragraph underneath it,</p> <p>14 one, two, three, four, five, six, seven,</p> <p>15 eight -- nine lines down there's a sentence</p> <p>16 that starts all the way to the right with the</p> <p>17 word "much" after a citation of Marselos and</p> <p>18 Tomatis.</p> <p>19 Do you see that, sir?</p> <p>20 A. Yes.</p> <p>21 MS. MILLER: I don't.</p> <p>22 MR. RESTAINO: Page 15,</p> <p>23 Chemicals and Hormonal Cancers,</p> <p>24 Jessica.</p> <p>25 MS. MILLER: Okay.</p>
<p style="text-align: right;">Page 119</p> <p>1 Q. I'm sorry, sir, I only asked</p> <p>2 again because you asked me to.</p> <p>3 MS. MILLER: Actually, that</p> <p>4 wasn't your last question. You had</p> <p>5 moved on from that.</p> <p>6 THE WITNESS: Yeah, it was a</p> <p>7 different question.</p> <p>8 MR. RESTAINO: Okay. I</p> <p>9 apologize.</p> <p>10 QUESTIONS BY MR. RESTAINO:</p> <p>11 Q. Do you rely upon the strength</p> <p>12 of association in determining causation?</p> <p>13 A. I think it's an important</p> <p>14 factor.</p> <p>15 (Boyd Exhibit 6 marked for</p> <p>16 identification.)</p> <p>17 QUESTIONS BY MR. RESTAINO:</p> <p>18 Q. I've now marked as Boyd 6 an</p> <p>19 article titled "Hormonal Carcinogenesis and</p> <p>20 Environmental Influences: Background and</p> <p>21 Overview," written by a James Huff, Jeff Boyd</p> <p>22 and J. Carl Barrett.</p> <p>23 Does that sound familiar, sir?</p> <p>24 A. Yes.</p> <p>25 Q. And if you would turn to</p>	<p style="text-align: right;">Page 121</p> <p>1 MR. RESTAINO: About 11 down.</p> <p>2 The word "much" is on the right-hand</p> <p>3 side following the citation.</p> <p>4 MS. MILLER: I see it.</p> <p>5 QUESTIONS BY MR. RESTAINO:</p> <p>6 Q. "Much of the stimulus for</p> <p>7 evaluating chemicals for potential</p> <p>8 carcinogenicity came from the revelation that</p> <p>9 DES caused cancer in both male and female</p> <p>10 human offspring whose women have been given</p> <p>11 DES to prevent or reduce threatened</p> <p>12 spontaneous abortion."</p> <p>13 And then there's several</p> <p>14 citations there, including Chapter 19 of the</p> <p>15 volume from which this paper came from.</p> <p>16 Did I read that correctly?</p> <p>17 A. Yes.</p> <p>18 Q. And you used -- you write there</p> <p>19 that "DES caused cancer," correct?</p> <p>20 A. Well, first of all, three of</p> <p>21 us, I being the middle author, were involved</p> <p>22 in the authorship of this article.</p> <p>23 So I'm sorry, but I -- I</p> <p>24 focused on the word "you," so I would</p> <p>25 respectfully ask you to repeat the question</p>

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<p style="text-align: right;">Page 122</p> <p>1 so that I may digest the full question.</p> <p>2 Q. As used here by yourself and</p> <p>3 your coauthors, "Much of the stimulus for</p> <p>4 evaluating chemicals for potential</p> <p>5 carcinogenicity came from the revelation that</p> <p>6 DES caused cancer in both male and female</p> <p>7 human offspring whose mother had been given</p> <p>8 DES to prevent or reduce threatened</p> <p>9 spontaneous abortion."</p> <p>10 Did I read it correctly?</p> <p>11 A. You read it correctly again,</p> <p>12 yes.</p> <p>13 Q. Okay. Now, Doctor, has the</p> <p>14 causal association between DES and clear cell</p> <p>15 adenocarcinoma ever been established in a</p> <p>16 randomized controlled trial?</p> <p>17 MS. MILLER: Objection.</p> <p>18 THE WITNESS: I'll just say no.</p> <p>19 QUESTIONS BY MR. RESTAINO:</p> <p>20 Q. Has the causal association</p> <p>21 between DES and clear cell adenocarcinoma</p> <p>22 ever been established in a cohort</p> <p>23 observational study?</p> <p>24 MS. MILLER: Objection.</p> <p>25 THE WITNESS: Could you repeat</p>	<p style="text-align: right;">Page 124</p> <p>1 misleading question.</p> <p>2 THE WITNESS: I would say no</p> <p>3 because -- for the primary reason that</p> <p>4 the -- the events were extraordinarily</p> <p>5 rare, and DES was on the market for</p> <p>6 pregnancy support for a relatively</p> <p>7 short period of time, late '40s until</p> <p>8 1971.</p> <p>9 It would be impossible to do</p> <p>10 such a study, in my mind, and have it</p> <p>11 significantly powered; hence the</p> <p>12 reliance on animal models over the</p> <p>13 years to provide much more rigorous</p> <p>14 evidence of causality with respect to</p> <p>15 DES and carcinogenicity.</p> <p>16 QUESTIONS BY MR. RESTAINO:</p> <p>17 Q. In fact, the initial</p> <p>18 association between DES and clear cell</p> <p>19 carcinoma -- adenocarcinoma in the offspring</p> <p>20 of women who took it, the drug, were</p> <p>21 established in case-control studies</p> <p>22 initially, correct?</p> <p>23 A. I'm of the -- I'm aware of the</p> <p>24 paper that I referenced earlier as being the</p> <p>25 first suggestion that there was an</p>
<p style="text-align: right;">Page 123</p> <p>1 the question, please?</p> <p>2 QUESTIONS BY MR. RESTAINO:</p> <p>3 Q. Yes.</p> <p>4 Has the causal association</p> <p>5 between DES and clear cell adenocarcinoma</p> <p>6 ever been established in a cohort</p> <p>7 observational study?</p> <p>8 A. Well, first of all, you're</p> <p>9 using the words "causal" and "association"</p> <p>10 together, which in my mind are different</p> <p>11 concepts.</p> <p>12 As I believe I suggested</p> <p>13 before, in my mind, epidemiologic studies,</p> <p>14 whether they be case-control or cohort</p> <p>15 studies, are typically relied upon to suggest</p> <p>16 associations leading to hypotheses that may</p> <p>17 be further tested regarding causation.</p> <p>18 So juxtaposing "association"</p> <p>19 and "causation" in the sentence is, in my</p> <p>20 mind, inappropriate.</p> <p>21 Q. Has the causal relationship</p> <p>22 between DES and clear cell adenocarcinoma</p> <p>23 ever been established in a cohort</p> <p>24 observational study?</p> <p>25 MS. MILLER: Objection. It's a</p>	<p style="text-align: right;">Page 125</p> <p>1 association.</p> <p>2 Q. Would you agree it would be</p> <p>3 inaccurate for anyone to say that causation</p> <p>4 cannot be established for the use of</p> <p>5 case-control studies?</p> <p>6 MS. MILLER: Objection.</p> <p>7 THE WITNESS: Several negatives</p> <p>8 in there.</p> <p>9 Could you repeat the question,</p> <p>10 please?</p> <p>11 QUESTIONS BY MR. RESTAINO:</p> <p>12 Q. Would you agree it would be</p> <p>13 inaccurate for one to say that a causal</p> <p>14 association between a substance or a drug and</p> <p>15 the development of cancer cannot be</p> <p>16 established through case-controlled,</p> <p>17 observational epidemiology?</p> <p>18 MS. MILLER: Objection.</p> <p>19 THE WITNESS: Well, first, I'm</p> <p>20 not an expert in epidemiology and</p> <p>21 the -- I'll stop there.</p> <p>22 QUESTIONS BY MR. RESTAINO:</p> <p>23 Q. Okay. You write on the bottom</p> <p>24 of page 2 of your expert report, the very</p> <p>25 last sentence --</p>

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<p style="text-align: right;">Page 126</p> <p>1 MS. MILLER: "Overall?"</p> <p>2 MR. RESTAINO: "Overall."</p> <p>3 QUESTIONS BY MR. RESTAINO:</p> <p>4 Q. The last sentence that goes on</p> <p>5 to page 3. "Overall, genetic predisposition</p> <p>6 is currently believed to be associated with</p> <p>7 approximately 20 percent of all ovarian</p> <p>8 cancers."</p> <p>9 Did I read that correctly?</p> <p>10 A. You read it correctly.</p> <p>11 Q. And then you then write, "It is</p> <p>12 very important to recognize that ovarian</p> <p>13 cancers associated with genetic</p> <p>14 predisposition, as well as those, open paren,</p> <p>15 approximately 80 percent, close paren, that</p> <p>16 occur, quote, sporadically, close paren, are</p> <p>17 all associated with the acquisition and</p> <p>18 accumulation of mutations affecting multiple</p> <p>19 cancer-related genes."</p> <p>20 Did I read that correctly, sir?</p> <p>21 A. You read it correctly.</p> <p>22 Q. And you do not have a reference</p> <p>23 for that opinion, do you?</p> <p>24 A. No.</p> <p>25 Q. The next sense -- next sentence</p>	<p style="text-align: right;">Page 128</p> <p>1 causal mechanism?</p> <p>2 MS. MILLER: Objection.</p> <p>3 THE WITNESS: I would disagree.</p> <p>4 That's a hugely, overly broad</p> <p>5 statement about cancers generally.</p> <p>6 QUESTIONS BY MR. RESTAINO:</p> <p>7 Q. Are you familiar with the term</p> <p>8 "gene environment interaction"?</p> <p>9 A. Yes.</p> <p>10 Q. And this means that an</p> <p>11 environmental factor's effect upon a body may</p> <p>12 depend upon a genetic factor; isn't that</p> <p>13 correct?</p> <p>14 A. Would you repeat the question,</p> <p>15 please?</p> <p>16 Q. That means that an</p> <p>17 environmental factor's effect on the body may</p> <p>18 depend upon a genetic factor; is that</p> <p>19 correct?</p> <p>20 A. Not really.</p> <p>21 Q. You can't think of any</p> <p>22 situations where that --</p> <p>23 A. No, I'm saying your -- your</p> <p>24 definition of the term is not really correct</p> <p>25 as I understand it.</p>
<p style="text-align: right;">Page 127</p> <p>1 you wrote, "In this sense, all ovarian</p> <p>2 cancers, open paren, and indeed all cancers</p> <p>3 generally, close paren, represent a genetic</p> <p>4 disease."</p> <p>5 Did I read that correctly?</p> <p>6 A. Yes, you did.</p> <p>7 Q. And again, there's no reference</p> <p>8 for that, correct?</p> <p>9 A. You are correct.</p> <p>10 Q. Now, are you familiar with the</p> <p>11 term "multicausality" as it relates to cancer</p> <p>12 development?</p> <p>13 A. No.</p> <p>14 Q. Are you associated with the</p> <p>15 term "multicausality" as it relates to any</p> <p>16 disease?</p> <p>17 A. I mean, I can infer what such a</p> <p>18 word might mean. I'm -- it's not a word I've</p> <p>19 ever used.</p> <p>20 Q. Okay.</p> <p>21 A. To the best of my knowledge.</p> <p>22 Q. As an expert in genetics, would</p> <p>23 you agree that it's reasonably safe to assume</p> <p>24 that there are nearly always some genetic and</p> <p>25 some environmental component causes in every</p>	<p style="text-align: right;">Page 129</p> <p>1 Q. Okay. Would you agree that a</p> <p>2 genetic factor's effect on the body may</p> <p>3 depend upon the environmental factor?</p> <p>4 A. Could you give me an example of</p> <p>5 an environmental factor in this particular</p> <p>6 case?</p> <p>7 I assume we're talking about --</p> <p>8 we're still talking about hereditary ovarian</p> <p>9 cancers?</p> <p>10 Q. We're just talking in general</p> <p>11 about the gene environment interaction right</p> <p>12 now and multicausality.</p> <p>13 So, for example, there are</p> <p>14 individuals who smoke 20 -- 20 cigarettes a</p> <p>15 day for 40 years and they develop lung</p> <p>16 cancer, correct?</p> <p>17 A. Correct.</p> <p>18 Q. And there are some individuals</p> <p>19 who smoke the exact same amount and they</p> <p>20 don't develop lung cancer?</p> <p>21 A. Correct.</p> <p>22 Q. And there are individuals that</p> <p>23 are exposed to chimney smoke and they don't</p> <p>24 develop cancer, testicular cancer, correct?</p> <p>25 A. Well, I assume you meant soot,</p>

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<p style="text-align: right;">Page 130</p> <p>1 but I'll -- assuming you agree with my 2 assumption as to your question, I would say 3 correct. 4 Q. In fact, 1975, Sir Percival 5 Pott first reported on the association 6 between kidney -- chimney soot and testicular 7 cancer, correct? 8 MS. MILLER: Objection. 9 THE WITNESS: No, he'd been 10 dead for 200 years in 1975. 11 QUESTIONS BY MR. RESTAINO: 12 Q. Okay. Regardless of his death, 13 do you recall Dr. Pott reporting on the 14 incidence of testicular cancer in chimney 15 sweeps? 16 MS. MILLER: Objection. 17 THE WITNESS: I recall Sir 18 Percival Pott reporting on an 19 association between scrotal cancer and 20 sweeping chimney -- chimneys. 21 QUESTIONS BY MR. RESTAINO: 22 Q. In fact, that may have been the 23 first reported association between an 24 environmental factor and the development of 25 cancer, agreed?</p>	<p style="text-align: right;">Page 132</p> <p>1 QUESTIONS BY MR. RESTAINO: 2 Q. You would agree, though, that 3 certain genes, such as BRCA1, BRCA2, can give 4 women an inherent susceptibility to breast 5 cancer, correct? 6 A. Inherent -- if we substitute 7 "inherit" for "inherent," I would agree with 8 that statement, yes. 9 MS. MILLER: I was about to 10 object to that word. You didn't give 11 me a chance. 12 THE WITNESS: Noted. 13 MS. MILLER: Did you mean 14 inherited, or did you mean inherent? 15 MR. RESTAINO: It's written 16 "inherited," and I think I misspoke. 17 MS. MILLER: Okay. 18 MR. RESTAINO: So I'll repeat 19 the question. 20 MS. MILLER: I didn't know what 21 you meant by "inherent," so -- 22 THE WITNESS: I know what you 23 meant, and so I'll -- 24 QUESTIONS BY MR. RESTAINO: 25 Q. Answer with the understanding</p>
<p style="text-align: right;">Page 131</p> <p>1 MS. MILLER: Objection. 2 THE WITNESS: No, I think 3 that's probably a reach. I think that 4 was an extraordinarily strong 5 association between an environmental 6 exposure and the development of a 7 cancer. 8 To the extent that it was the 9 first report, I really couldn't say. 10 QUESTIONS BY MR. RESTAINO: 11 Q. Okay. As you sit here today, 12 can you think of a prior environmental 13 exposure report leading to increased risk of 14 cancer in people? 15 A. Prior to the 18th century? 16 Q. Yes. 17 A. No. 18 Q. Well, would you agree -- or do 19 you have an opinion to a reasonable degree of 20 medical certainty or scientific certainty as 21 to what percentage of cancer in this country 22 are related to environmental factors? 23 MS. MILLER: Objection. 24 THE WITNESS: No. 25</p>	<p style="text-align: right;">Page 133</p> <p>1 it was inherited? 2 A. Correct. 3 Q. And in fact, the inherited 4 mutations in BRCA1, BRCA2 also confer a 5 predisposition to ovarian cancer in some 6 women, correct? 7 A. That's correct. 8 Q. But not everyone who has the 9 BRCA1 and BRCA2 mutation develops breast 10 cancer or ovarian cancer, correct? 11 A. Correct. 12 Q. Would you agree or disagree 13 that the general consensus of the medical 14 community is that many cancers are 15 environmentally caused? 16 A. I would disagree. There's 17 absolutely no evidence to support that 18 statement as you read it, today as we sit 19 here. 20 Q. Today has it changed, in your 21 opinion? 22 A. Yes, I think it has. 23 Q. And when do you think it 24 changed? 25 A. I think it changed dramatically</p>

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<p style="text-align: right;">Page 134</p> <p>1 in the late 1970s when Bishop and Varmus made</p> <p>2 their seminal observation that human beings</p> <p>3 had, within their genome, cells that in a</p> <p>4 retroviral-induced context caused cancer in</p> <p>5 chickens, leading to the ultimate realization</p> <p>6 that cancer in humans is a result of</p> <p>7 mutations in genes within the cells of our</p> <p>8 various organs and tissues.</p> <p>9 Q. Okay.</p> <p>10 A. Prior to 1978 when those</p> <p>11 seminal publications were published, we spent</p> <p>12 a lot of time looking for links between the</p> <p>13 environment and cancer, a lot of time looking</p> <p>14 for links between viruses and cancer.</p> <p>15 We -- in a very general sense</p> <p>16 "we," the field -- spent a lot of time</p> <p>17 looking for anything that could explain</p> <p>18 cancer pathogenesis. And that was really a</p> <p>19 transformational event, a true inflection</p> <p>20 point in our understanding of cancer</p> <p>21 pathogenesis in humans generally, the</p> <p>22 understanding that the aberrant regulation or</p> <p>23 mutation of cells in one or another tissue</p> <p>24 was in fact the driving force of cancer</p> <p>25 development in most cases of cancer. There</p>	<p style="text-align: right;">Page 136</p> <p>1 Do you see that, sir?</p> <p>2 A. Cancer Causality and Etiology,</p> <p>3 yes.</p> <p>4 Q. And then underneath that, you,</p> <p>5 Dr. Huff and Dr. Barrett write, "Identifiable</p> <p>6 causes of most human cancers unfortunately</p> <p>7 remain unknown, yet the general consensus</p> <p>8 appears to be that many are, quote,</p> <p>9 environmentally caused and hence should be</p> <p>10 preventable."</p> <p>11 Did I read that correctly?</p> <p>12 A. You read it correctly.</p> <p>13 Q. And that was published by</p> <p>14 Drs. Huff, yourself and Barrett in "Cellular</p> <p>15 and Molecular Mechanisms of Hormonal</p> <p>16 Carcinogenesis: Environmental Influences,"</p> <p>17 1996; is that correct?</p> <p>18 A. Yes. 20, 30 years ago.</p> <p>19 Q. And in the next paragraph you</p> <p>20 wrote, "Known causes of cancer include both</p> <p>21 external factors, open paren, tobacco smoke,</p> <p>22 chemicals, occupational exposure</p> <p>23 circumstances, radiation, viruses, close</p> <p>24 paren, and internal factors, open paren,</p> <p>25 hormones, immune conditions, inherited genes,</p>
<p style="text-align: right;">Page 135</p> <p>1 are exceptions, of course.</p> <p>2 Q. And this was prior to 1978?</p> <p>3 A. No, the inflection point was</p> <p>4 1978, and I was talking about subsequent.</p> <p>5 Q. Okay.</p> <p>6 A. Following 1978 where the whole</p> <p>7 notion of cancer genes took root, catalyzed,</p> <p>8 again, a virtual transformational period</p> <p>9 involving our understanding of the driving</p> <p>10 force of cancer development.</p> <p>11 Q. If you would turn again to I</p> <p>12 think it's the last exhibit, which is 6, the</p> <p>13 paper by James Huff and yourself and Carl</p> <p>14 Barrett, and turn to page 11?</p> <p>15 A. This is Exhibit 5, correct?</p> <p>16 No. I'm sorry, I'm on my --</p> <p>17 Q. I think it's 6.</p> <p>18 A. Exhibit 6, you're correct. I</p> <p>19 had my --</p> <p>20 Q. That's quite all right.</p> <p>21 A. -- expert report.</p> <p>22 Q. There's a section there called</p> <p>23 Cancer Causality and Etiology.</p> <p>24 A. Which page, please?</p> <p>25 Q. Page 11.</p>	<p style="text-align: right;">Page 137</p> <p>1 close paren, as well as aging," which we</p> <p>2 discussed earlier, correct?</p> <p>3 MS. MILLER: Is there a</p> <p>4 question there?</p> <p>5 QUESTIONS BY MR. RESTAINO:</p> <p>6 Q. Did I read that correctly?</p> <p>7 A. You read it correctly.</p> <p>8 MS. MILLER: Except to that</p> <p>9 which we had discussed earlier.</p> <p>10 That's not in here.</p> <p>11 QUESTIONS BY MR. RESTAINO:</p> <p>12 Q. Now, Doctor, a moment ago or</p> <p>13 some time ago, I did -- I asked you about the</p> <p>14 concept of multifactorial disease.</p> <p>15 Do you recall that?</p> <p>16 A. I do.</p> <p>17 Q. Would you agree that there are</p> <p>18 multiple biologically plausible risk factors</p> <p>19 for the development of ovarian cancer?</p> <p>20 MS. MILLER: Objection.</p> <p>21 I think the witness testified</p> <p>22 earlier that he doesn't think</p> <p>23 biologically plausible is -- I just</p> <p>24 want to get exactly right what he</p> <p>25 said.</p>

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<p style="text-align: right;">Page 138</p> <p>1 THE WITNESS: I can answer it 2 again. 3 MS. MILLER: Okay. 4 THE WITNESS: I don't equate 5 association with causality. 6 QUESTIONS BY MR. RESTAINO: 7 Q. Okay. Would you agree that 8 there are risk factors that are associated 9 with an increased risk for the development of 10 ovarian cancer? 11 A. Yes. 12 Q. Would that include, stating the 13 obvious, gender? 14 A. Yes. 15 Q. Age over 45? 16 A. Yes. 17 Q. How about a woman who has not 18 had a tubal ligation, does that increase the 19 risk? 20 A. I wouldn't phrase it that way, 21 no. 22 Q. How would you phrase it? 23 A. I would say that tubal ligation 24 decreases the risk. 25 Q. Okay. How about no</p>	<p style="text-align: right;">Page 140</p> <p>1 A. Nulliparity is a risk factor 2 for ovarian cancer. 3 Q. Would no oral contraceptive use 4 be a risk factor for the development of 5 ovarian cancer? 6 MS. MILLER: Objection. 7 THE WITNESS: I disagree with 8 the statement. 9 QUESTIONS BY MR. RESTAINO: 10 Q. Is a positive family history of 11 ovarian cancer a risk factor for the 12 development of ovarian cancer? 13 A. I would suggest that a family 14 history involving first degree-relatives is a 15 risk factor for the development of ovarian 16 cancer. 17 Q. Would you agree that a woman 18 who has early onset breast cancer is at 19 increased risk for the development of ovarian 20 cancer? 21 MS. MILLER: Objection. 22 THE WITNESS: Yes, but I'd like 23 to qualify my answers to all of these 24 questions with respect to the 25 magnitude of risk, because it differs</p>
<p style="text-align: right;">Page 139</p> <p>1 breastfeeding, would that be a risk or a 2 protective factor? 3 MS. MILLER: Objection. 4 THE WITNESS: Well, to the 5 extent that parity reduces risk and 6 breast cancer -- or breast -- I'm 7 sorry, breastfeeding is almost always 8 associated with having children, I 9 would agree that breastfeeding is 10 associated with a reduced risk of 11 developing ovarian cancer. 12 QUESTIONS BY MR. RESTAINO: 13 Q. And the flip side, would no 14 breastfeeding, no live births, be a risk 15 factor for the development of ovarian cancer? 16 MS. MILLER: Objection. 17 THE WITNESS: I -- live births? 18 That's a little confusing to me. 19 QUESTIONS BY MR. RESTAINO: 20 Q. Full-term delivery of a baby. 21 A. We're going to have to start 22 over with the question. I'm sorry. 23 Q. Do you believe that no -- that 24 with no live births would be a risk factor 25 for the development of ovarian cancer?</p>	<p style="text-align: right;">Page 141</p> <p>1 with all of the risk factors that 2 we've just articulated over a period 3 of -- 4 QUESTIONS BY MR. RESTAINO: 5 Q. And I apologize. I should have 6 said this at the outset. 7 During the deposition I get to 8 ask my questions, and sometimes it's a yes or 9 no, disagree or agree answer. 10 At the end of the deposition, 11 the attorneys representing Johnson & Johnson 12 get to also ask you questions. So if there 13 are questions that you want -- answers you 14 want to expand upon, you will have time to do 15 that at the end of the deposition. 16 MS. MILLER: I think he can 17 also expand upon his answers during 18 the deposition in order to give full, 19 complete answers. 20 MR. RESTAINO: Not if the 21 witness is going to come out with 22 "fourscore and seven years ago" like 23 Dr. Shih. We're just not going down 24 that route today. 25 MS. MILLER: I see.</p>

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<p style="text-align: right;">Page 142</p> <p>1 QUESTIONS BY MR. RESTAINO: 2 Q. Doctor, is the use of oral -- 3 A. I'm sorry, perhaps I 4 misunderstood the ground rules. 5 In my mind, an answer is an 6 answer. 7 Q. Yes, I like to go by that, too. 8 So if I ask you if you agree or disagree, 9 it's a simple answer: "agree" or "disagree." 10 If you want to expand upon it, 11 then you'll have your opportunity at the end 12 of the deposition. 13 MS. MILLER: If you do not feel 14 that agree or disagree is a complete 15 and full and honest answer, then you 16 should give a full, complete and 17 honest answer. 18 QUESTIONS BY MR. RESTAINO: 19 Q. Doctor, would you agree that 20 the use of oral contraceptives are a 21 protective factor regarding ovarian cancer? 22 MS. MILLER: Are we talking 23 about all ovarian cancer? Are you 24 just talking about a specific ovarian 25 cancer?</p>	<p style="text-align: right;">Page 144</p> <p>1 of oral contraceptives for five years 2 or more is an especially strong 3 association which differs from the 4 magnitude of many risks that we've 5 previously discussed. 6 QUESTIONS BY MR. RESTAINO: 7 Q. Doctor, sitting here today in 8 2019, in addition to age over 45, no tubal 9 ligation, no breastfeeding, no live births, 10 oral contraceptive use, Jewish ethnicity, 11 family history of ovarian cancer, early onset 12 of breast cancer, would you add long-term 13 genital talcum powder to the list of risk 14 factors for the development of cancer, 15 ovarian cancer? 16 A. No. 17 Q. And why is that? 18 A. It's twofold. At best, the 19 epidemiologic association is quite weak, and 20 no biological plausibility. 21 Q. How are you defining biological 22 plausibility now? 23 MS. MILLER: Objection. 24 THE WITNESS: I define 25 biological plausibility now as I</p>
<p style="text-align: right;">Page 143</p> <p>1 I just want to make sure we're 2 all on the same page here. 3 MR. RESTAINO: Ovarian cancer 4 as in -- we're talking about in this 5 litigation and what's been discussed 6 in Dr. Saed's report and the 7 biological plausibility of plaintiff 8 experts referring to ovarian cancer. 9 QUESTIONS BY MR. RESTAINO: 10 Q. Would the use of oral 11 contraceptive be considered a protective 12 factor? 13 A. Would you like to finish the 14 question? 15 Q. Would the use of oral 16 contraceptives be considered a protective 17 factor for the development of ovarian cancer? 18 MS. MILLER: Objection. 19 THE WITNESS: The use of oral 20 contraceptives confers a decreased 21 risk of developing epithelial ovarian 22 carcinoma, including all its 23 histologic variants. 24 And I might add that the 25 decreased risk associated with the use</p>	<p style="text-align: right;">Page 145</p> <p>1 define it always, which is in essence 2 the articulation of a cogent mechanism 3 that gets you from a weak association 4 to causality. 5 QUESTIONS BY MR. RESTAINO: 6 Q. How do you define a cogent? 7 A. I think a cogent mechanism, it 8 needs to be clear as opposed to muddled, I 9 think it needs to be logical as opposed to 10 illogical, and I think it needs to be 11 compelling as opposed to speculative. 12 Q. Can it be possible? 13 A. Can what be possible? 14 MS. MILLER: Objection. 15 QUESTIONS BY MR. RESTAINO: 16 Q. A cogent biological 17 plausibility. 18 A. I'm sorry, sir, I've lost you 19 completely. 20 Q. Using the word "cogent" for 21 biological plausibility, can that be a 22 possible cause or risk factor? 23 A. I'm sorry, I just can't begin 24 to interpret your question. 25 Q. What part of it can't you</p>

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<p style="text-align: right;">Page 146</p> <p>1 interpret?</p> <p>2 A. The sentence doesn't make sense</p> <p>3 to me.</p> <p>4 Q. Okay.</p> <p>5 A. The question doesn't make</p> <p>6 sense.</p> <p>7 Q. We've defined cogent as you use</p> <p>8 it, correct?</p> <p>9 Biological plausibility. How</p> <p>10 do you define the English word</p> <p>11 "plausibility"?</p> <p>12 MS. MILLER: Objection. Asked</p> <p>13 and answered.</p> <p>14 THE WITNESS: The same as I</p> <p>15 would define biological plausibility,</p> <p>16 leaving out biological and applying</p> <p>17 plausibility to any other context.</p> <p>18 QUESTIONS BY MR. RESTAINO:</p> <p>19 Q. So if the -- if the dictionary</p> <p>20 defines plausibility as possible, and we add</p> <p>21 biological in front of it, as you just put,</p> <p>22 then we're talking about biological</p> <p>23 possibility, correct?</p> <p>24 MS. MILLER: Objection.</p> <p>25 THE WITNESS: No, I think we're</p>	<p style="text-align: right;">Page 148</p> <p>1 A. You read it correctly.</p> <p>2 Q. And have you performed any</p> <p>3 experiments to rule out talcum powder as one</p> <p>4 of the unknown causes of the somatic genetic</p> <p>5 mutations leading to ovarian cancer?</p> <p>6 MS. MILLER: Objection.</p> <p>7 THE WITNESS: It's impossible</p> <p>8 to perform a negative experiment.</p> <p>9 QUESTIONS BY MR. RESTAINO:</p> <p>10 Q. Have you performed any</p> <p>11 experiments to determine whether talcum</p> <p>12 powder was a cause of any of the somatic</p> <p>13 genetic mutations leading to ovarian cancer?</p> <p>14 A. You'd have to describe the</p> <p>15 context.</p> <p>16 Q. The context of this sentence,</p> <p>17 sir.</p> <p>18 "The context of the causes of</p> <p>19 somatic genetic mutations acquired in the</p> <p>20 organ in which a cancer ultimately develops</p> <p>21 remain largely unknown for ovarian cancer and</p> <p>22 most other cancers."</p> <p>23 In attempt to learn the</p> <p>24 unknown, have you -- have you attempted any</p> <p>25 experiments utilizing talcum powder and see</p>
<p style="text-align: right;">Page 147</p> <p>1 playing word games, and I just -- I</p> <p>2 just can't -- I'm not going to play</p> <p>3 syntax games with you.</p> <p>4 QUESTIONS BY MR. RESTAINO:</p> <p>5 Q. I'm just trying to ascertain or</p> <p>6 learn your definition so that as the day goes</p> <p>7 on I can use your definitions and words.</p> <p>8 A. And I'm quite confident that I</p> <p>9 offered my best definition for biological</p> <p>10 plausibility at least once, perhaps twice.</p> <p>11 Q. Okay. If you turn now to</p> <p>12 page 3 of your expert report and to the top</p> <p>13 paragraph, approximately eight lines down</p> <p>14 there's a sentence that you write that starts</p> <p>15 on the left with, "The causes of these</p> <p>16 somatic genetic mutations."</p> <p>17 Just let me know when you find</p> <p>18 that, sir.</p> <p>19 A. I've found it.</p> <p>20 Q. "The causes of these, quote,</p> <p>21 somatic, end quote, genetic mutations</p> <p>22 acquired in the organ in which a cancer</p> <p>23 ultimately develops remain largely unknown</p> <p>24 for ovarian cancer and most other cancers."</p> <p>25 Did I read that correctly?</p>	<p style="text-align: right;">Page 149</p> <p>1 the effect on somatic genetic mutations</p> <p>2 leading to ovarian cancer?</p> <p>3 MS. MILLER: Objection.</p> <p>4 THE WITNESS: I'll give it a</p> <p>5 shot.</p> <p>6 I used the word "organ" in the</p> <p>7 sentence, so I have to assume I was</p> <p>8 talking about animals or humans as</p> <p>9 opposed to, for example, cells.</p> <p>10 And I can state unequivocally</p> <p>11 that I've never treated animals or</p> <p>12 humans with talcum powder in order to</p> <p>13 see what might happen.</p> <p>14 QUESTIONS BY MR. RESTAINO:</p> <p>15 Q. Several sentences down, the</p> <p>16 same paragraph on the right-hand side --</p> <p>17 actually, it's one, two, three -- seven lines</p> <p>18 up from the bottom, approximately, there's a</p> <p>19 sentence that starts on the far right with</p> <p>20 "possible mutagenic."</p> <p>21 Do you see that, sir?</p> <p>22 A. Uh-huh, yes.</p> <p>23 Q. "Possible mutagenic mechanisms</p> <p>24 in ovarian and other cancer types include</p> <p>25 unknown environmental exposures and pure</p>

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<p style="text-align: right;">Page 150</p> <p>1 chance."</p> <p>2 Did I read that correctly?</p> <p>3 A. You read it correctly.</p> <p>4 Q. Is it your opinion at this time</p> <p>5 that the possible mutagenic mechanisms in</p> <p>6 ovarian and other cancer types, including</p> <p>7 unknown -- include unknown environmental</p> <p>8 exposures, but you're not willing at this</p> <p>9 time to access -- access -- accept the</p> <p>10 possibility of talcum powder being one of</p> <p>11 those environmental factors?</p> <p>12 MS. MILLER: Objection.</p> <p>13 Is this sentence -- is the</p> <p>14 question over?</p> <p>15 MR. RESTAINO: The question is</p> <p>16 over.</p> <p>17 MS. MILLER: All right.</p> <p>18 Objection.</p> <p>19 THE WITNESS: Well, here, my</p> <p>20 goal in writing this sentence was to</p> <p>21 refer to all cancer types, and so I</p> <p>22 was trying to make that transition</p> <p>23 from ovarian to all cancer types.</p> <p>24 QUESTIONS BY MR. RESTAINO:</p> <p>25 Q. Well --</p>	<p style="text-align: right;">Page 152</p> <p>1 genetic alterations in both oncogenes and</p> <p>2 tumor suppressor genes for their development.</p> <p>3 That is the transformation of a completely</p> <p>4 normal cell into a completely malignant cell</p> <p>5 capable of metastasizing.</p> <p>6 So I'm now speaking broadly</p> <p>7 about all cancers, widely accepted as a</p> <p>8 paradigm in the dictionary sense of what a</p> <p>9 paradigm is. And my goal here was to say in</p> <p>10 some cases -- let's pick a cancer, cervical</p> <p>11 cancer, where HPV infection is recognized as</p> <p>12 a causal factor.</p> <p>13 The reason we recognize it as a</p> <p>14 causal factor is we know that the human</p> <p>15 papilloma virus contains two transforming</p> <p>16 proteins known as E6 and E7. E6 binds to and</p> <p>17 activates the TP53 protein. E7 binds to and</p> <p>18 activates the RB1 tumor suppressor protein.</p> <p>19 And to the extent that the p53</p> <p>20 gene, when active, protects against the</p> <p>21 accumulation of spontaneous genetic damage,</p> <p>22 and RB1, when it's functioning normally,</p> <p>23 prevents inappropriate cell proliferation,</p> <p>24 the loss of constraints on cell proliferation</p> <p>25 and the loss of the so-called guardian of the</p>
<p style="text-align: right;">Page 151</p> <p>1 A. The --</p> <p>2 Q. I'm sorry.</p> <p>3 A. The paragraph is rather -- is</p> <p>4 rather a narrative of the, as we sit here</p> <p>5 today, commonly accepted essence of cancer</p> <p>6 development, which is the acquisition and</p> <p>7 accumulation of genetic mutations in</p> <p>8 oncogenes and tumor suppressor genes,</p> <p>9 regardless of the cancer type, ovarian and</p> <p>10 others. And in some cancer types, we have a</p> <p>11 pretty good idea of what the causes of those</p> <p>12 mutations are.</p> <p>13 In a, quote/unquote, hereditary</p> <p>14 context, the first rate-limiting genetic</p> <p>15 alteration is the mutant gene inherited from</p> <p>16 mom or dad.</p> <p>17 The subsequent genetic</p> <p>18 alterations are acquired -- the subsequent</p> <p>19 necessary genetic alterations are acquired</p> <p>20 somatically, getting back to your question of</p> <p>21 why don't all women with the BRCA1 or 2</p> <p>22 mutation develop breast or ovarian cancer.</p> <p>23 The one genetic mutation is insufficient for</p> <p>24 the development of cancer.</p> <p>25 All cancers require multiple</p>	<p style="text-align: right;">Page 153</p> <p>1 genome p53 lead to subsequent mutations,</p> <p>2 requisite, as I indicated, for all cancers.</p> <p>3 And that's a very good example</p> <p>4 of knowing how a particular exogenous agent</p> <p>5 is both highly associated, indeed 100 percent</p> <p>6 associated, with all squamous carcinomas of</p> <p>7 the cervix and indeed causal based on a deep</p> <p>8 knowledge of the biological mechanism.</p> <p>9 We don't know as much about</p> <p>10 many other cancers as we do about cervical</p> <p>11 cancer. And that's the point I was trying to</p> <p>12 make with this paragraph.</p> <p>13 Q. We're going to return to the</p> <p>14 HPV virus and cancer.</p> <p>15 Suffice to say right now that</p> <p>16 there are many versions of HPV virus,</p> <p>17 correct? Many?</p> <p>18 A. Many isoforms? Isotypes?</p> <p>19 Q. Yes.</p> <p>20 A. Yes, and two are particularly</p> <p>21 carcinogenic.</p> <p>22 Q. And some are not?</p> <p>23 A. Well --</p> <p>24 Q. But we will return to that in a</p> <p>25 moment.</p>

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<p style="text-align: right;">Page 154</p> <p>1 A. I'll grant you that.</p> <p>2 MS. MILLER: Is that a</p> <p>3 question? I mean, is that a question,</p> <p>4 or is that just a statement?</p> <p>5 THE WITNESS: I think it was</p> <p>6 a --</p> <p>7 MS. MILLER: Let's only answer</p> <p>8 questions, not statements.</p> <p>9 QUESTIONS BY MR. RESTAINO:</p> <p>10 Q. What you wrote here, sir, was</p> <p>11 "possible mutagenic mechanisms in ovarian and</p> <p>12 other cancer types include unknown</p> <p>13 environmental exposures and pure chance."</p> <p>14 My question to you is: Of the</p> <p>15 possible mutagenic mechanisms in ovarian</p> <p>16 cancer, including unknown environmental</p> <p>17 exposures, you are not willing at this time</p> <p>18 to accept the possibility of talcum powder</p> <p>19 being one of those factors; is that correct?</p> <p>20 A. That's correct.</p> <p>21 MS. MILLER: Objection.</p> <p>22 THE WITNESS: Sorry.</p> <p>23 QUESTIONS BY MR. RESTAINO:</p> <p>24 Q. And then you write, the next</p> <p>25 sentence, "Indeed, one prominent cancer</p>	<p style="text-align: right;">Page 156</p> <p>1 MS. MILLER: Objection.</p> <p>2 THE WITNESS: You read what I</p> <p>3 wrote correctly.</p> <p>4 QUESTIONS BY MR. RESTAINO:</p> <p>5 Q. Okay. And you did not put in</p> <p>6 that paragraph any of the subsequent</p> <p>7 arguments made following the publication of</p> <p>8 Tomasetti, et al., in Nature, did you?</p> <p>9 A. No, I didn't.</p> <p>10 Q. In addition to Tomasetti and</p> <p>11 Vogelstein, did you review article by Martin</p> <p>12 Nowak and -- I'm not even going to pronounce</p> <p>13 this doctor's last name. It's W-a-c-l-a-w --</p> <p>14 Waclaw, perhaps, titled "Genes, Environment,</p> <p>15 and, quote, Bad Luck, end quote," explaining</p> <p>16 cancer risk in a statistical sense, published</p> <p>17 in Science in March 2017?</p> <p>18 A. Perhaps.</p> <p>19 Could you show me the paper,</p> <p>20 please.</p> <p>21 Q. Absolutely, sir. I'm marking</p> <p>22 it now as Boyd 7.</p> <p>23 (Boyd Exhibit 7 marked for</p> <p>24 identification.)</p> <p>25</p>
<p style="text-align: right;">Page 155</p> <p>1 molecular geneticist recently posited that</p> <p>2 most cancer cases may simply be attributable</p> <p>3 to bad luck, hyphen, genetic mutations</p> <p>4 resulting from chance, errors, in the</p> <p>5 ordinary replication of the cellular genome,</p> <p>6 open paren, 3.3 billion base pairs per cell,</p> <p>7 close paren, whenever one cell divides into</p> <p>8 two. Reference number 4."</p> <p>9 Did I read that correctly?</p> <p>10 A. You read it correctly.</p> <p>11 Q. And how do you define bad luck?</p> <p>12 A. It was an unfortunate term, and</p> <p>13 Dr. Vogelstein received a lot of criticism</p> <p>14 for his use of the term "bad luck."</p> <p>15 But I think he would have been</p> <p>16 better served having used the term</p> <p>17 "stochastic."</p> <p>18 Q. But, sir, in your expert report</p> <p>19 you don't say that it's an unfortunate term,</p> <p>20 nor do you say that you received controversy.</p> <p>21 What you do say is one</p> <p>22 prominent cancer molecular geneticist</p> <p>23 recently posited that most cancer cases may</p> <p>24 simply be attributable to bad luck; isn't</p> <p>25 that correct?</p>	<p style="text-align: right;">Page 157</p> <p>1 QUESTIONS BY MR. RESTAINO:</p> <p>2 Q. And as you see in the far lower</p> <p>3 right-hand corner, this is published in</p> <p>4 Science.</p> <p>5 Would you agree that Science is</p> <p>6 a highly rated scientific journal?</p> <p>7 MS. MILLER: Objection.</p> <p>8 THE WITNESS: I don't rate</p> <p>9 scientific journals. I rate the</p> <p>10 science in the journals.</p> <p>11 QUESTIONS BY MR. RESTAINO:</p> <p>12 Q. First paragraph, Drs. Nowak and</p> <p>13 Waclaw write, "It is a human trait to search</p> <p>14 for explanations for catastrophic events and</p> <p>15 rule out mere, quote, chance, end quote, or,</p> <p>16 quote, bad luck, end quote, when it comes to</p> <p>17 human cancer, but the issue of natural causes</p> <p>18 versus bad luck was raised by Tomasetti and</p> <p>19 Vogelstein about two years ago, open paren</p> <p>20 number 1. Their study, which was widely</p> <p>21 misinterpreted as saying that most cancers</p> <p>22 are due neither to genetic inheritance nor</p> <p>23 environmental factors but simply bad luck</p> <p>24 sparked controversy."</p> <p>25 Did I read that correctly?</p>

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<p style="text-align: right;">Page 158</p> <p>1 A. You read it correctly.</p> <p>2 Q. Would you agree the Tomasetti</p> <p>3 and Vogelstein paper, when it was published,</p> <p>4 sparked controversy?</p> <p>5 A. My memory is that the use of</p> <p>6 the term "bad luck" sparked controversy.</p> <p>7 That was the essence of the uproar.</p> <p>8 Q. Would you agree controversy, in</p> <p>9 essence, means two or more differing</p> <p>10 viewpoints?</p> <p>11 A. That totally depends on the</p> <p>12 context.</p> <p>13 Q. In this context, would you</p> <p>14 agree there was a controversy as to whether</p> <p>15 there was bad luck involved or not bad luck</p> <p>16 involved?</p> <p>17 MS. MILLER: Objection. Vague.</p> <p>18 THE WITNESS: As I indicated</p> <p>19 earlier, it's my memory that the</p> <p>20 controversy in this particular case</p> <p>21 had to do with syntax. Both the</p> <p>22 scientific community and the public</p> <p>23 community were uncomfortable with the</p> <p>24 use of the term "bad luck."</p> <p>25</p>	<p style="text-align: right;">Page 160</p> <p>1 today, the underlying essence of</p> <p>2 cancer pathogenicity, generally</p> <p>3 speaking, which is an extraordinarily</p> <p>4 challenging task in one paragraph.</p> <p>5 And so, yes, there are</p> <p>6 textbooks -- and I'm holding my</p> <p>7 fingers approximately six inches</p> <p>8 apart -- having to do with the</p> <p>9 pathogenicity of human cancer. And so</p> <p>10 in attempting to distill the knowledge</p> <p>11 that the scientific and medical</p> <p>12 communities hold today regarding the</p> <p>13 pathogenicity of human cancer</p> <p>14 generally, I did indeed leave out a</p> <p>15 lot.</p> <p>16 QUESTIONS BY MR. RESTAINO:</p> <p>17 Q. It was not your intention to</p> <p>18 distill to the judge that may have been</p> <p>19 reading your expert report that some women</p> <p>20 develop ovarian cancer strictly through bad</p> <p>21 luck, was it?</p> <p>22 MS. MILLER: Objection.</p> <p>23 THE WITNESS: It was my</p> <p>24 intention to explain to whoever may</p> <p>25 read this expert report that one</p>
<p style="text-align: right;">Page 159</p> <p>1 QUESTIONS BY MR. RESTAINO:</p> <p>2 Q. And that's the totality of your</p> <p>3 understanding of the controversy?</p> <p>4 A. Yes, it is.</p> <p>5 Q. You don't discuss the</p> <p>6 controversy in your expert report when</p> <p>7 stating that one prominent molecular</p> <p>8 geneticist published on bad luck, do you?</p> <p>9 MS. MILLER: Objection. Asked</p> <p>10 and answered.</p> <p>11 QUESTIONS BY MR. RESTAINO:</p> <p>12 Q. Do you?</p> <p>13 A. No. And I would only add that</p> <p>14 there are many things that I don't state in</p> <p>15 my expert report.</p> <p>16 Q. Somewhere in your -- I'm sorry.</p> <p>17 Somewhere in your expert</p> <p>18 report --</p> <p>19 MS. MILLER: I think he was in</p> <p>20 the middle of a sentence.</p> <p>21 MR. RESTAINO: I'm sorry, I</p> <p>22 thought I heard a period.</p> <p>23 THE WITNESS: You know, again,</p> <p>24 the purpose of this paragraph was an</p> <p>25 attempt to distill, as we sit here</p>	<p style="text-align: right;">Page 161</p> <p>1 hypothesis regarding the cause of the</p> <p>2 requisite genetic mutations and</p> <p>3 cancers generally may be stochastic</p> <p>4 errors in DNA replication during the</p> <p>5 process of normal cell division.</p> <p>6 QUESTIONS BY MR. RESTAINO:</p> <p>7 Q. Maybe equate to possibility?</p> <p>8 MS. MILLER: Objection.</p> <p>9 THE WITNESS: Well, if we're</p> <p>10 going -- again, could you read back my</p> <p>11 answer, please, and see what he's</p> <p>12 equating to what?</p> <p>13 I would like my answer to stand</p> <p>14 as I -- you're asking me to redefine a</p> <p>15 term I used in answering your</p> <p>16 question, and I would prefer not to</p> <p>17 redefine terms that I've used in</p> <p>18 answering your question.</p> <p>19 QUESTIONS BY MR. RESTAINO:</p> <p>20 Q. Well, when you say that it may</p> <p>21 be somatically particular errors in DNA</p> <p>22 replication -- and I'm just asking there,</p> <p>23 inasmuch as you used the word "may" -- does</p> <p>24 that equate to possibly?</p> <p>25 MS. MILLER: Objection.</p>

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<p style="text-align: right;">Page 162</p> <p>1 THE WITNESS: We're actually</p> <p>2 debating as to whether "may" is</p> <p>3 synonymous with "possibly"?</p> <p>4 QUESTIONS BY MR. RESTAINO:</p> <p>5 Q. How would you use may? With</p> <p>6 probable? Certainly?</p> <p>7 MS. MILLER: Objection.</p> <p>8 QUESTIONS BY MR. RESTAINO:</p> <p>9 Q. I'm just trying to use your</p> <p>10 words.</p> <p>11 MS. MILLER: Objection. He</p> <p>12 gave his words.</p> <p>13 THE WITNESS: I gave you my</p> <p>14 words.</p> <p>15 (Boyd Exhibit 8 marked for</p> <p>16 identification.)</p> <p>17 QUESTIONS BY MR. RESTAINO:</p> <p>18 Q. May. Okay.</p> <p>19 Let's turn to a paper that</p> <p>20 we've now marked and handed to you titled</p> <p>21 "Substantial Contribution of Extrinsic Risk</p> <p>22 Factors to Cancer Development," lead author</p> <p>23 Song Wu, W-u, published in Nature in June</p> <p>24 of 2016.</p> <p>25 Do you have that, sir?</p>	<p style="text-align: right;">Page 164</p> <p>1 percent, close paren, to cancer development.</p> <p>2 First, we demonstrate that the correlation</p> <p>3 between stem-cell division and cancer risk</p> <p>4 does not distinguish between the effects of</p> <p>5 intrinsic and extrinsic factors. Next, we</p> <p>6 show that intrinsic risk is better estimated</p> <p>7 by the lower bound risk controlling for total</p> <p>8 stem cell divisions. Finally, we show that</p> <p>9 the rates of endogenous mutation accumulation</p> <p>10 by intrinsic processes are not sufficient to</p> <p>11 account for the observed cancer risk.</p> <p>12 Collectively, we conclude that cancer risk is</p> <p>13 heavily influenced by intrinsic factors.</p> <p>14 These results may carry immense consequences</p> <p>15 for strategizing cancer prevention, research</p> <p>16 and public health."</p> <p>17 Did I read that correctly?</p> <p>18 A. You read it correctly.</p> <p>19 Q. Now, Doctor, safe to say that</p> <p>20 you did not reference this paper by Wu, et</p> <p>21 al., in your expert report, correctly --</p> <p>22 correct?</p> <p>23 MS. MILLER: Objection.</p> <p>24 THE WITNESS: You are correct</p> <p>25 that I did not reference this article.</p>
<p style="text-align: right;">Page 163</p> <p>1 A. I just want to make sure that</p> <p>2 Ms. Miller has a copy and that I have a</p> <p>3 copy --</p> <p>4 MS. MILLER: I do. We both</p> <p>5 have copies.</p> <p>6 THE WITNESS: -- and that we're</p> <p>7 not taking each other's copies.</p> <p>8 MS. MILLER: I'm not going to</p> <p>9 steal your copy, I promise.</p> <p>10 THE WITNESS: I believe your</p> <p>11 question was, do I have that paper.</p> <p>12 Yes, I do.</p> <p>13 QUESTIONS BY MR. RESTAINO:</p> <p>14 Q. And if you take a look at the</p> <p>15 summary written on the first page, "Recent</p> <p>16 research has highlighted a strong correlation</p> <p>17 between tissue-specific cancer risk and the</p> <p>18 lifetime number of tissue-specific stem cell</p> <p>19 divisions. Whether such correlation implies</p> <p>20 a high, unavoidable, intrinsic cancer risk</p> <p>21 has become a key public health debate with</p> <p>22 dissemination of the, quote -- or bad luck,</p> <p>23 quote, hypothesis. Here, we provide evidence</p> <p>24 that intrinsic risk factors contribute only</p> <p>25 modestly, open paren, less than 10 to 30</p>	<p style="text-align: right;">Page 165</p> <p>1 QUESTIONS BY MR. RESTAINO:</p> <p>2 Q. And if you turn to page 2, sir,</p> <p>3 the top paragraph, the first full sentence</p> <p>4 after references numbers 6 and 7, "Much</p> <p>5 discussion has been made."</p> <p>6 Do you see where I am, sir?</p> <p>7 A. Yes.</p> <p>8 Q. "Much discussion has been made</p> <p>9 to argue against the bad luck hypothesis,</p> <p>10 references 5 to 13, yet none offered specific</p> <p>11 alternatives to quantifiably evaluate the</p> <p>12 contribution of extrinsic risk factors in</p> <p>13 cancer development. Applying several</p> <p>14 distinct modeling approaches, we here provide</p> <p>15 strong evidence that unavoidable, intrinsic</p> <p>16 risk factors contribute only modestly, open</p> <p>17 paren, less than 10 to approximately 20,</p> <p>18 30 percent, close paren, to the development</p> <p>19 of many common cancers."</p> <p>20 Did I read that correctly?</p> <p>21 A. You did.</p> <p>22 Q. So, Doctor, other than writing</p> <p>23 "Indeed, one prominent cancer molecular</p> <p>24 geneticist recently posited that most cancer</p> <p>25 cases can simply be attributable to bad</p>

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<p style="text-align: right;">Page 166</p> <p>1 luck," you do not provide any references in 2 your expert report regarding follow-up 3 publications which argue against the bad luck 4 hypotheses; is that correct? 5 MS. MILLER: Objection. 6 THE WITNESS: That is correct. 7 And I would add that my purpose 8 in attempting to distill the great 9 body of knowledge that currently 10 exists as we sit here today as to the 11 etiology in general of all cancers in 12 general, I'm sure I left out thousands 13 of, if not hundreds of thousands, of 14 publications. 15 My purpose was to distill a 16 large body of evidence using an 17 example. 18 QUESTIONS BY MR. RESTAINO: 19 Q. Doctor, are you familiar with 20 the term "confirmation bias"? 21 MS. MILLER: Objection. 22 THE WITNESS: That strikes me 23 as an epidemiologic/statistical term, 24 and I'm not prepared to discuss 25 statistical, epidemiologic concepts.</p>	<p style="text-align: right;">Page 168</p> <p>1 housekeeping or do you want to... 2 MR. RESTAINO: Yeah, this is a 3 good time by me. 4 MS. MILLER: Great. 5 THE WITNESS: I'm sorry, are we 6 done with Huff, Boyd and Barrett? 7 MR. RESTAINO: Yes, sir. 8 THE WITNESS: Thank you. 9 VIDEOGRAPHER: Off the record 10 at 12:36 p.m. 11 (Off the record at 12:36 p.m.) 12 VIDEOGRAPHER: We are back on 13 record at 1:10 p.m. 14 QUESTIONS BY MR. RESTAINO: 15 Q. Welcome back, Dr. Boyd. And as 16 we were discussing off the record, however, 17 the same thing applies: If you need or want 18 anytime to take a break, you get to call 19 timeout at any time. 20 A. Thank you. 21 Q. You're welcome. 22 Now, Doctor, I have marked as 23 Exhibit 9 -- we only have a couple copies. 24 MR. RESTAINO: Do you have a -- 25 copies of the e-mails?</p>
<p style="text-align: right;">Page 167</p> <p>1 QUESTIONS BY MR. RESTAINO: 2 Q. In non-epidemiological, 3 statistical parlance, are you familiar with 4 the concept of cherry-picking papers, studies 5 or articles that support your point of view? 6 A. Cherry-picking is indeed a 7 colloquialism I'm familiar with, and I'm 8 certain you're going to point out where I 9 used it in my expert report. 10 But, yes, I'm familiar with the 11 term. 12 Q. Okay. If you would turn now to 13 your expert report, the bottom of page 3, 14 there's a Section 4 down there. 15 A. Okay. Let's see, we've got -- 16 Q. And, Doctor, I'll withdraw that 17 statement for a moment. I'll just let you 18 know I think we're all done with Wu and 19 Nowak, if you want to get it out of your way, 20 and just keep your expert report -- 21 A. Thank you. 22 Q. -- just for housekeeping 23 purposes. 24 MS. MILLER: Is this a good 25 time to break for lunch if we're</p>	<p style="text-align: right;">Page 169</p> <p>1 MS. MILLER: Uh-huh. 2 QUESTIONS BY MR. RESTAINO: 3 Q. And, Doctor, did you get a 4 chance to look at these e-mails during the 5 lunch break? 6 A. I flipped through them. It was 7 a large stack, but, yes, I had a chance to 8 look at them. 9 Q. Do they refresh your memory at 10 all regarding e-mail, telephone and physical 11 meetings with Dr. Emmel and another attorney 12 in or about March of 2017? 13 A. It refreshes my memory about 14 e-mails and a telephone conversation with a 15 female attorney and possibly someone else, 16 but, I'm sorry, I have absolutely no 17 recollection of a face-to-face meeting. 18 (Boyd Exhibit 9 marked for 19 identification.) 20 QUESTIONS BY MR. RESTAINO: 21 Q. Okay. Do you have any 22 recollection whatsoever of a telephonic 23 communication? 24 A. Yes. 25 Q. And do you recall at that time</p>

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<p style="text-align: right;">Page 170</p> <p>1 sharing with Dr. Emmel and anyone else who 2 might have been on the phone your opinion 3 regarding the biological plausibility of 4 talcum powder and ovarian cancer? 5 A. Not specifically. I can only 6 presume in my strongest, albeit vague, memory 7 of the discourse was that I wasn't their guy. 8 Q. Did you -- 9 A. After I understood which side 10 of the argument plaintiffs' attorneys were 11 on. And I think that was a mutual agreement 12 between presumably the woman to your right 13 and myself. 14 Q. Okay. I have marked these 15 e-mails as 9, and I'll just put them here for 16 the court reporter. 17 One other thing which I should 18 have said in the beginning, and it always 19 makes for fun at the end of the deposition: 20 The documents with the orange sticker on them 21 have to go with him, so we can't take our 22 copies. So if you have some in a pile, let's 23 be careful with them. 24 Okay? 25 A. I'm sorry. Him? Her?</p>	<p style="text-align: right;">Page 172</p> <p>1 I read that correctly? 2 A. Both. 3 Q. Thank you. 4 Yet when I asked you earlier 5 about your keywords that you utilized in 6 conducting your search of the biomedical 7 literature for your report, you didn't 8 include inflammation in those -- that list of 9 keywords; is that correct? 10 A. Yes, but I modified my answer 11 to that question by explaining that I did get 12 around to looking at papers relating 13 inflammation to -- ostensibly to talc 14 exposure and ovarian cancer by virtue of 15 having read thoroughly the various documents 16 that we've discussed multiple times now 17 relating to Dr. Saed, his paper, his 18 deposition, his expert report and so forth. 19 Q. Okay. Well, now, Doctor, I'm 20 just going to ask you to jump ahead, and then 21 we'll come back down. But if you go to 22 page 18 of your report, and on the final 23 paragraph you start off with, "Finally, 24 Dr. Saed." 25 Do you see that, sir, the last</p>
<p style="text-align: right;">Page 171</p> <p>1 Q. Her. 2 A. Her. 3 Q. Yes, I'm sorry. 4 A. You want to leave them out 5 there? 6 Q. Probably safe. We don't need 7 it. 8 A. Okay. 9 Q. Now, if you return to your 10 expert report at the bottom of page 3, 11 there's a Section 4. 12 Do you see that, sir? 13 A. Yes. 14 Q. In the first sentence you 15 write, "Plaintiff experts propose that talc 16 causes inflammation, which leads to cancer, 17 or that inflammation causes oxidative stress, 18 which damages DNA, which results in cancer." 19 And did I read that correctly? 20 A. Yes, you did. 21 Q. And in the next sentence you 22 write, "These explanations are simplistic, 23 speculative and lacks sufficient scientific 24 support to be deemed plausible." 25 Did I read that carefully? Did</p>	<p style="text-align: right;">Page 173</p> <p>1 paragraph? 2 A. Uh-huh. Yes. 3 Q. "Finally, Dr. Saed appears to 4 take for granted that ovarian cancer is 5 caused by inflammation, but this, too, has 6 not been established. Dr. Saed essentially 7 ignores the body of science suggesting that 8 chronic inflammation does not play a role in 9 the development of ovarian, reference 82, as 10 well as studies that considered whether 11 aspirin use and anti-inflammatory drugs 12 reduced the risk of ovarian, reference 83, 13 with mixed results." 14 And did I read that correctly? 15 A. More or less, but I submit that 16 you read it correctly. 17 Q. Okay. Thank you. 18 Now, Doctor, did you ignore the 19 body of science suggesting that chronic 20 inflammation does, in fact, play a role in 21 the development of ovarian cancer? 22 MS. MILLER: Objection. 23 THE WITNESS: I didn't 24 consciously ignore anything. 25</p>

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<p style="text-align: right;">Page 174</p> <p>1 QUESTIONS BY MR. RESTAINO: 2 Q. Well, you ignored the Nowak 3 editorial and the Wu paper that conflicted 4 with your opinion that cancer can be caused 5 by bad luck, did you not? 6 MS. MILLER: Wait a minute. 7 Where does he say he has the opinion 8 that cancer can be caused by bad luck? 9 What are you talking about? 10 That was a sentence that said, 11 "indeed, one scientist." 12 QUESTIONS BY MR. RESTAINO: 13 Q. One prominent geneticist plays 14 into bad luck -- 15 MS. MILLER: Has posited. 16 QUESTIONS BY MR. RESTAINO: 17 Q. And that's what you wrote, 18 correct? 19 A. Could you please ask the 20 question? 21 Q. Well, I'll strike that 22 question. 23 MS. MILLER: Good idea. 24 MR. RESTAINO: The record will 25 stand on itself.</p>	<p style="text-align: right;">Page 176</p> <p>1 would you agree? 2 A. That's -- I would -- I would 3 suggest that if I did a PubMed search, a 4 Googlian search, with ovarian, capital A, 5 capital N, capital D, cancer, there may be 50 6 to a hundred thousand papers that might pop 7 up. 8 Q. So how did you select the ones 9 that you were going to rely upon for your 10 expert report? 11 A. Because it's necessary to parse 12 a hundred thousand papers into those that are 13 particularly relevant to the hypothesis 14 currently being litigated. 15 Q. And did you parse the hundred 16 thousand papers into those that supported 17 your opinions in this regard and were in 18 conflict with your opinions in this regard? 19 MS. MILLER: Objection. 20 THE WITNESS: First of all, 21 100,000 is just an extraordinarily 22 general estimate, but I would be happy 23 to allow any of you to type in 24 "ovarian" and "cancer" and see what 25 comes up in PubMed and we can get to</p>
<p style="text-align: right;">Page 175</p> <p>1 (Boyd Exhibit 10 marked for 2 identification.) 3 QUESTIONS BY MR. RESTAINO: 4 Q. Now, Doctor, I've marked as 5 Boyd 10 a paper titled "C-reactive Protein as 6 Independent Prognostic Variable in Patients 7 with Ovarian Cancer." Lead author is Hefler, 8 H-e-f-l-e-r, published in Clinical Cancer 9 Research, 2008. 10 Have you seen this paper 11 before, Doctor? 12 A. If I have, I don't -- it's all 13 the same. I don't remember seeing it, no. 14 Q. Okay. I'll represent to you 15 that it's not referenced in your expert 16 report. 17 A. Thank you. 18 Q. And, Doctor, the title contains 19 the words "ovarian cancer," correct? 20 A. The title does contain the 21 words "ovarian cancer." 22 Q. So if one was conducting a 23 narrative search of the biomedical literature 24 using keywords "ovarian" and "cancer," then 25 one would expect this paper to come up also;</p>	<p style="text-align: right;">Page 177</p> <p>1 an exact number, but I don't think 2 that's the issue. 3 With respect to your -- the 4 second part of your question, it's my 5 experience as a biomedical researcher 6 over however many years it's been, 35, 7 that papers' titles are more often 8 than not agnostic to the conclusion 9 reached. 10 And so if I'm going to select, 11 based on a PubMed search which 12 includes titles and authors, which 13 papers to read, at the end of the day, 14 it's pretty much a random process. 15 QUESTIONS BY MR. RESTAINO: 16 Q. Well, suffice to say, you did 17 not select this paper to read, correct? 18 A. I don't remember reading it, 19 that is correct. 20 Q. Okay. And if you would look at 21 the abstract, see they write, "Purpose: To 22 evaluate serum C-reactive protein, open 23 paren, CRP, close paren, as prognostic 24 variable in patients with epithelial ovarian 25 cancer, open paren, EOC, close paren." The</p>

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<p style="text-align: right;">Page 178</p> <p>1 experimental design, that this was "a 2 multi-center study. Preoperative serum CRP 3 was evaluated in 623 patients with EOC. 4 Results were correlated with clinical data." 5 And if you go jump down to the 6 conclusion they write, "Serum CRP can be seen 7 as a novel, widely available, independent 8 prognostic available of ovarian cancer." 9 Did I read that carefully? 10 A. Close enough. 11 Q. Okay. Thank you. 12 So now if you'd look at -- on 13 the first page, in the right column, the very 14 first paragraph, they -- starts off with "the 15 pathogenesis and development of ovarian 16 cancer." 17 Have you seen that? 18 A. Yes. 19 Q. And they write, "The 20 pathogenesis of ovarian cancer -- and 21 development of ovarian cancer have also been 22 closely linked to inflammatory processes, 23 open paren, 6, 7, close paren." 24 Did I read that carefully? 25 MS. MILLER: Did you read it</p>	<p style="text-align: right;">Page 180</p> <p>1 in the history of cancer as centuries go. 2 (Boyd Exhibit 11 marked for 3 identification.) 4 QUESTIONS BY MR. RESTAINO: 5 Q. The reference 7 I've now marked 6 as Boyd 11. It's "Inflammation and Cancer: 7 Back to Virchow." And if you -- if you look 8 down at the lower left, it states that -- all 9 the way down at the bottom -- this was 10 published in the Lancet in 2001; is that 11 correct? 12 A. That is correct. 13 Q. And do you recognize the Lancet 14 as a premier medical journal in the world? 15 MS. MILLER: Objection. 16 THE WITNESS: I recognize the 17 Lancet as a British Medical Journal. 18 QUESTIONS BY MR. RESTAINO: 19 Q. Okay. Do you know what its 20 impact factor is? 21 A. No. 22 Q. Do you know what an impact 23 factor is? 24 A. Yes. 25 Q. Okay. If I represent to you</p>
<p style="text-align: right;">Page 179</p> <p>1 carefully? 2 MR. RESTAINO: Correctly. I'm 3 going to say that all afternoon. 4 THE WITNESS: Yes. 5 QUESTIONS BY MR. RESTAINO: 6 Q. Thank you. 7 And in fact, references 6 and 8 7, if you go to the back, 6 is by the author 9 H-e-l-z-l-s-o-u-e-r, et al., and 7 is 10 Balkwill, Mantovani, "Inflammation and 11 Cancer: Back to Virchow." 12 Did I read that correctly? Or 13 carefully? 14 A. Both. 15 Q. Are you familiar with 16 Dr. Rudolf Virchow, or Virchow? 17 A. I've never met the man. He's 18 been dead for a long time. 19 Q. Yes. 20 But are you familiar with his 21 work? 22 A. I'm relatively -- cottonmouth 23 thing again. Excuse me. 24 I'm relatively familiar with 25 the fact that he was a rather iconic figure</p>	<p style="text-align: right;">Page 181</p> <p>1 that the Lancet has an impact factor of 2 53.24, would that indicate that it has high 3 esteem as a medical journal? 4 A. It would indicate that papers 5 published in that journal are frequently 6 referenced by others. 7 Q. Okay. And the lead author is 8 Fran Balkwill. 9 Do you know her? 10 A. We've met. 11 Q. Have you ever published with 12 her? 13 A. I'm guessing the answer is yes. 14 Q. If -- guessing or estimating? 15 I'll withdraw it. 16 If you turn to the second 17 page -- 18 A. Of? 19 Q. -- of the Balkwill and 20 Mantovani paper. 21 A. Oh, the Lancet. 22 Q. The Lancet paper, okay. 23 And you see they have a -- I'm 24 sorry, it's actually page 541 -- no, excuse 25 me. Give me one moment. I appear to have</p>

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<p style="text-align: right;">Page 182</p> <p>1 marked my...</p> <p>2 Very sorry. Right there in</p> <p>3 front of me.</p> <p>4 The first page, in the lower</p> <p>5 right-hand corner, there's a panel 1:</p> <p>6 Sub-associations between inflammation and</p> <p>7 cancer risk.</p> <p>8 Do you see that, sir?</p> <p>9 A. I do.</p> <p>10 Q. And on the left they list</p> <p>11 malignancy and on the right inflammatory</p> <p>12 stimulus\condition.</p> <p>13 Do you see that, sir?</p> <p>14 A. Yes.</p> <p>15 Q. And if you see the third line</p> <p>16 down under malignancy is listed ovarian. And</p> <p>17 to the right they have pelvic inflammatory</p> <p>18 disease\talc\tissue remodeling.</p> <p>19 Did I read that correctly?</p> <p>20 A. You did.</p> <p>21 Q. So as these authors published</p> <p>22 in Lancet in 2001, talc was listed as one of</p> <p>23 the inflammatory stimuli or conditions which</p> <p>24 could cause ovarian cancer; is that correct?</p> <p>25 MS. MILLER: Objection.</p>	<p style="text-align: right;">Page 184</p> <p>1 they're simply restating the large</p> <p>2 epidemiologic literature that pertains to</p> <p>3 that putative risk.</p> <p>4 Q. Actually, in this area they</p> <p>5 were talking about, Doctor, focusing on the</p> <p>6 role of inflammation, especially chronic</p> <p>7 inflammation, and the development of cancer,</p> <p>8 it is -- we discussed where you wrote that</p> <p>9 "Dr. Saed appears to take for granted that</p> <p>10 ovarian cancer is caused by inflammation,</p> <p>11 but, this, too, has not been established.</p> <p>12 Dr. Saed essentially ignores the body of</p> <p>13 science suggesting that chronic inflammation</p> <p>14 does not play a role in the development of</p> <p>15 ovarian cancer."</p> <p>16 So with that in mind, if you</p> <p>17 look to the left of -- in the left column of</p> <p>18 the Balkwill Lancet paper, the second</p> <p>19 paragraph, you see it starts off "panel 1"?</p> <p>20 So it's left column, front</p> <p>21 page of the Lancet article.</p> <p>22 A. Do you mean right column?</p> <p>23 Q. Left column, second</p> <p>24 paragraph --</p> <p>25 A. Oh, the text that says "panel</p>
<p style="text-align: right;">Page 183</p> <p>1 THE WITNESS: No, that's not</p> <p>2 correct.</p> <p>3 QUESTIONS BY MR. RESTAINO:</p> <p>4 Q. What's incorrect about that?</p> <p>5 A. Panel 1 seems to be a summary</p> <p>6 of their impression of the literature</p> <p>7 suggesting that talc is one of several</p> <p>8 associations that have been noticed -- that</p> <p>9 have been noted with, in this particular</p> <p>10 case, ovarian cancer risk. It has nothing to</p> <p>11 do with -- I mean, this is, after all, a</p> <p>12 review article, and so everything in here is</p> <p>13 a summary of other -- I mean, it's not a</p> <p>14 primary paper.</p> <p>15 Q. In your --</p> <p>16 A. So in other words, Dr. Balkwill</p> <p>17 and her colleague are not providing evidence</p> <p>18 that -- primary evidence that talc is</p> <p>19 associated with ovarian cancer risk. They're</p> <p>20 simply pointing out something that I believe</p> <p>21 we've already agreed to: that there is</p> <p>22 indeed, at least to the extent that I</p> <p>23 understand it, a weak association,</p> <p>24 epidemiologic association, between perineal</p> <p>25 talc use and ovarian cancer risk. And</p>	<p style="text-align: right;">Page 185</p> <p>1 1." Yes.</p> <p>2 Q. Yes.</p> <p>3 "Panel 1 lists some cancers</p> <p>4 where the inflammatory process is a cofactor</p> <p>5 in carcinogenesis."</p> <p>6 Did I read that correctly?</p> <p>7 A. You did.</p> <p>8 Q. And this goes back to, again,</p> <p>9 2001, agreed?</p> <p>10 A. The paper was published in</p> <p>11 2001, yes.</p> <p>12 Q. Now, if you look at the</p> <p>13 abstract, seven lines down, sort of to the</p> <p>14 left, second word, there's a -- the -- first</p> <p>15 there's a word "cancer," and then "if genetic</p> <p>16 damage."</p> <p>17 Do you see that, sir?</p> <p>18 A. Yes.</p> <p>19 Q. "If genetic damage is the,</p> <p>20 quote, match that lights the fire, end quote,</p> <p>21 of cancer, some types of inflammation may</p> <p>22 provide the, quote, fuel that feeds the</p> <p>23 flames, end quote."</p> <p>24 Did I read that correctly?</p> <p>25 A. You did.</p>

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<p>1 Q. And this was published in a</p> <p>2 peer-reviewed publication in 2001, correct?</p> <p>3 A. It's a review article that was</p> <p>4 published in a peer-reviewed publication in</p> <p>5 2001, that is correct.</p> <p>6 Q. And a review article is meant</p> <p>7 to put together the literature for readers so</p> <p>8 that if one wants to look up a topic, it</p> <p>9 could be a good starting point for studying</p> <p>10 that topic; would you agree?</p> <p>11 MS. MILLER: Objection.</p> <p>12 THE WITNESS: I know what my</p> <p>13 purpose in writing a review article</p> <p>14 is. I can't opine on Dr. Balkwill's</p> <p>15 goals in writing a review article.</p> <p>16 (Boyd Exhibit 12 marked for</p> <p>17 identification.)</p> <p>18 QUESTIONS BY MR. RESTAINO:</p> <p>19 Q. Okay. I've now marked as</p> <p>20 Boyd 12 an article written by Roberta Ness,</p> <p>21 Carrie Cottreau, titled "Possible Role of</p> <p>22 Ovarian Epithelial Inflammation in Ovarian</p> <p>23 Cancer." This was published in the Journal</p> <p>24 of the National Cancer Institute in 1999.</p> <p>25 Do you see the -- do you</p>	<p>1 don't know what month it was</p> <p>2 published, so I was being generous.</p> <p>3 THE WITNESS: Well, it's fair</p> <p>4 to say that it was submitted several</p> <p>5 months before it was ever published,</p> <p>6 but regardless, I honestly don't</p> <p>7 remember the paper.</p> <p>8 QUESTIONS BY MR. RESTAINO:</p> <p>9 Q. I understand. I'm just asking</p> <p>10 if you remember.</p> <p>11 A. No, I don't.</p> <p>12 Q. You've met Dr. Ness, though. I</p> <p>13 think that's what you've just testified to?</p> <p>14 A. Yes.</p> <p>15 Q. And do you hold her in high</p> <p>16 esteem as a research scientist?</p> <p>17 MS. MILLER: Objection.</p> <p>18 THE WITNESS: I don't hold</p> <p>19 individuals in high or low or any</p> <p>20 esteem in terms of research. I prefer</p> <p>21 to look at the research itself as</p> <p>22 opposed to making some kind of</p> <p>23 judgment about the quality of an</p> <p>24 individual that produced it.</p> <p>25</p>
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<p>1 recognize the Journal of the National Cancer</p> <p>2 Institute as a highly respected medical</p> <p>3 journal?</p> <p>4 A. I recognize it as a</p> <p>5 peer-reviewed journal.</p> <p>6 Q. You have six publications in</p> <p>7 this journal yourself, do you not?</p> <p>8 A. I couldn't tell you. Or I'm</p> <p>9 unable to tell you.</p> <p>10 Q. Okay. Do you know Dr. Roberta</p> <p>11 Ness?</p> <p>12 A. We've met.</p> <p>13 Q. In fact, you've published with</p> <p>14 her, correct?</p> <p>15 A. That's something I'll take your</p> <p>16 word for. I'm sure you're correct.</p> <p>17 Q. Does the paper "Ovarian Cancer</p> <p>18 in High Risk Women: Implications for</p> <p>19 Prevention, Screening and Early Detection,"</p> <p>20 published in Gynecologic Oncology in 2003</p> <p>21 ring a bell, appreciating that it was</p> <p>22 15 years ago?</p> <p>23 MS. MILLER: 16. It's 2019,</p> <p>24 John.</p> <p>25 MR. RESTAINO: Yeah, but we</p>	<p>1 QUESTIONS BY MR. RESTAINO:</p> <p>2 Q. Okay. The paper by Dr. Ness</p> <p>3 and Dr. Cottreau is "Possible Role of Ovarian</p> <p>4 Epithelial Inflammation in Ovarian Cancer,"</p> <p>5 correct?</p> <p>6 A. Still is.</p> <p>7 Q. So we have the words "ovarian,"</p> <p>8 "inflammation" and "cancer" in the title.</p> <p>9 Did you see this article when</p> <p>10 you did your PubMed review of the biomedical</p> <p>11 literature?</p> <p>12 A. I think I may have.</p> <p>13 Q. And did you review this</p> <p>14 article?</p> <p>15 A. I may have read the abstract.</p> <p>16 Q. Well, let's look at the</p> <p>17 abstract then.</p> <p>18 And if you look on the third</p> <p>19 line, starting on the right, "This paper</p> <p>20 reviews the epidemiologic literature in the</p> <p>21 English language on risk factors and</p> <p>22 protective factors for ovarian cancer and</p> <p>23 proposes a novel hypothesis that a common</p> <p>24 mechanism underlying this disease is</p> <p>25 inflammation. Previous hypothesis about the</p>

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<p style="text-align: right;">Page 190</p> <p>1 causes of ovarian cancer have attributed risk</p> <p>2 to an excess number of lifetime ovulations or</p> <p>3 to elevations in steroid hormones.</p> <p>4 Inflammation may underlie ovulatory events</p> <p>5 because an inflammatory reaction is induced</p> <p>6 during the process of ovulation. Additional</p> <p>7 risk factors for ovarian cancer, including</p> <p>8 asbestos and talc exposure, endometriosis,</p> <p>9 open paren, i.e., ectopic implantation of</p> <p>10 uterine lining tissue, close paren, and</p> <p>11 pelvic inflammatory disease, cannot be</p> <p>12 directly linked to ovulation or to hormones</p> <p>13 but do cause pelvic -- local pelvic</p> <p>14 inflammation."</p> <p>15 Did I read this correctly?</p> <p>16 A. Yes.</p> <p>17 Q. Now, do you have the</p> <p>18 physiological expertise to opine on whether</p> <p>19 inflammatory reaction is induced during the</p> <p>20 process of ovulation?</p> <p>21 A. I don't and -- I'm sorry, could</p> <p>22 you repeat the sentence?</p> <p>23 Q. Do you have the physiological</p> <p>24 expertise to opine on whether an inflammatory</p> <p>25 reaction is induced during the process of</p>	<p style="text-align: right;">Page 192</p> <p>1 I think if there were a</p> <p>2 substantial body of experimental data</p> <p>3 demonstrating that inflammation was due --</p> <p>4 produced during the process of human</p> <p>5 ovulation, I would like to see it.</p> <p>6 Throughout this -- the large</p> <p>7 body of this abstract that you just read, she</p> <p>8 used the word "hypothesis" multiple times.</p> <p>9 And I think these are interesting hypotheses.</p> <p>10 My opinion sitting here today</p> <p>11 is that we, the scientific community, really</p> <p>12 have no idea why the ovulatory process</p> <p>13 repeated to an excess as opposed to a lesser</p> <p>14 degree is associated with an increased risk</p> <p>15 of ovarian cancer.</p> <p>16 Q. When you say "we, the</p> <p>17 scientific community," would it surprise you</p> <p>18 to understand that there are other members of</p> <p>19 the scientific community that disagree with</p> <p>20 you in that regard?</p> <p>21 A. That there are data from</p> <p>22 humans -- and this is a question. That there</p> <p>23 are data from humans, human tissues, showing</p> <p>24 that ovulation produces an inflammatory</p> <p>25 response in the ovary?</p>
<p style="text-align: right;">Page 191</p> <p>1 ovulation?</p> <p>2 MS. MILLER: Objection.</p> <p>3 THE WITNESS: Physiologic</p> <p>4 expertise is kind of a weird term.</p> <p>5 I think what you mean to say</p> <p>6 is, do I have the expertise to opine</p> <p>7 on whether --</p> <p>8 QUESTIONS BY MR. RESTAINO:</p> <p>9 Q. On whether an inflammatory</p> <p>10 reaction is induced during ovulation?</p> <p>11 A. I think what you're asking is,</p> <p>12 do I have the expertise to opine on whether</p> <p>13 an inflammatory process is induced during the</p> <p>14 process of ovulation.</p> <p>15 I think expertise is really the</p> <p>16 wrong term here. I think -- I think if there</p> <p>17 were evidence -- I'll start over.</p> <p>18 I think -- I'll start over.</p> <p>19 I know that incessant ovulation</p> <p>20 and all the risk factors and protective</p> <p>21 factors that are associated with incessant</p> <p>22 ovulation, or lack thereof, are to one degree</p> <p>23 or another risk factors for ovarian cancer.</p> <p>24 I believe that. And I think I'm qualified to</p> <p>25 believe that, as we've discussed all morning.</p>	<p style="text-align: right;">Page 193</p> <p>1 Q. Yes.</p> <p>2 A. I would like to see the data.</p> <p>3 Q. You haven't to date?</p> <p>4 A. No.</p> <p>5 Q. Okay. Do you agree with</p> <p>6 Dr. Roberta Ness and Carrie Cottreau when</p> <p>7 they describe asbestos as an additional risk</p> <p>8 factor for ovarian cancer?</p> <p>9 MS. MILLER: Objection. I</p> <p>10 think he said he wasn't offering</p> <p>11 opinions on asbestos.</p> <p>12 MR. RESTAINO: I'm not asking</p> <p>13 if he's got an opinion on asbestos.</p> <p>14 I'm asking if he agrees with this</p> <p>15 published opinion.</p> <p>16 THE WITNESS: Well, if I'm not</p> <p>17 offering an opinion, I'm not going to</p> <p>18 offer an opinion on someone else's</p> <p>19 opinion.</p> <p>20 QUESTIONS BY MR. RESTAINO:</p> <p>21 Q. Okay.</p> <p>22 A. With all due respect.</p> <p>23 Q. Well, do you agree with</p> <p>24 Dr. Roberta Ness and Carrie Cottreau when</p> <p>25 they describe talc exposure as an additional</p>

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<p style="text-align: right;">Page 194</p> <p>1 risk factor for ovarian cancer?</p> <p>2 MS. MILLER: Can you point him</p> <p>3 to what you're talking about?</p> <p>4 THE WITNESS: It's further down</p> <p>5 in the abstract. I'll find it.</p> <p>6 Perhaps further up. Perhaps</p> <p>7 right in the middle.</p> <p>8 Okay. Now I found the</p> <p>9 sentence. Can you please repeat the</p> <p>10 question?</p> <p>11 QUESTIONS BY MR. RESTAINO:</p> <p>12 Q. Do you agree with Drs. Roberta</p> <p>13 Ness and Carrie Cottreau when they describe</p> <p>14 talc exposure as an additional risk factor</p> <p>15 for ovarian cancer?</p> <p>16 MS. MILLER: Objection.</p> <p>17 THE WITNESS: Yeah, I think</p> <p>18 we've covered this multiple times. I</p> <p>19 will agree that there is a limited</p> <p>20 body of weak -- there's a limited body</p> <p>21 of evidence suggesting a very weak</p> <p>22 risk in terms of association of talc</p> <p>23 with ovarian cancer.</p> <p>24 QUESTIONS BY MR. RESTAINO:</p> <p>25 Q. And how do you define very weak</p>	<p style="text-align: right;">Page 196</p> <p>1 A. The population risk of ovarian</p> <p>2 cancer, the general population risk, is</p> <p>3 approximately 1.3. So in other words, 1 out</p> <p>4 of 87 women over a lifetime will develop</p> <p>5 ovarian cancer.</p> <p>6 And so if the relative risk</p> <p>7 associated with a particular exposure is</p> <p>8 increased by 30 percent, when you multiply</p> <p>9 1.3 times 1.3 and you get the risk associated</p> <p>10 with -- again, if we accept the relative risk</p> <p>11 of 1.3, you get the risk associated with talc</p> <p>12 exposure from the association studies.</p> <p>13 Q. Isn't it true that if one is</p> <p>14 looking for an increased risk in a</p> <p>15 population, the background rate from which we</p> <p>16 start is limited to unity or 1.0?</p> <p>17 MS. MILLER: Objection.</p> <p>18 THE WITNESS: 1.0 equals 1.3,</p> <p>19 but I'll stop there. I'm getting out</p> <p>20 of my realm of expertise.</p> <p>21 QUESTIONS BY MR. RESTAINO:</p> <p>22 Q. Okay. If you look at the final</p> <p>23 two sentences of the abstract in the paper by</p> <p>24 Ness and Cottreau, they write, "Inflammation</p> <p>25 entails cell damage."</p>
<p style="text-align: right;">Page 195</p> <p>1 risk in terms of association?</p> <p>2 A. A risk factor of, for example,</p> <p>3 1.2 or 1.3. A relative risk of 1.2 or 1.3.</p> <p>4 Q. I thought you testified earlier</p> <p>5 that you were not an expert in epidemiology.</p> <p>6 Do you understand what a risk</p> <p>7 ratio of 1.2 to 1.3 can equate to --</p> <p>8 MS. MILLER: Objection.</p> <p>9 QUESTIONS BY MR. RESTAINO:</p> <p>10 Q. -- as far as causation?</p> <p>11 MS. MILLER: Objection.</p> <p>12 THE WITNESS: 1.3 times 1.3.</p> <p>13 QUESTIONS BY MR. RESTAINO:</p> <p>14 Q. Do you know how that equates to</p> <p>15 risk?</p> <p>16 A. Yeah. 1.3 is the general</p> <p>17 population risk, times 1.3, would give you</p> <p>18 your increased risk with a relative risk of</p> <p>19 1.3.</p> <p>20 Q. Where are you getting that</p> <p>21 from?</p> <p>22 A. Is that a rhetorical question?</p> <p>23 Q. No.</p> <p>24 What's the basis for that</p> <p>25 opinion?</p>	<p style="text-align: right;">Page 197</p> <p>1 Do you see that down there,</p> <p>2 sir?</p> <p>3 A. I'm sorry, where are we?</p> <p>4 Q. It's approximately five or six</p> <p>5 lines up from the bottom of the abstract.</p> <p>6 "Inflammation entails cell damage" --</p> <p>7 Do you see that?</p> <p>8 A. I see it.</p> <p>9 Q. -- "oxidative stress, elevation</p> <p>10 of cytokines and prostaglandins, all of which</p> <p>11 may be mutagenic. The possibility that</p> <p>12 inflammation is a pathophysiologic</p> <p>13 contributor to the development of ovarian</p> <p>14 cancer suggests a directed approach to future</p> <p>15 research."</p> <p>16 Did I read that correctly?</p> <p>17 A. You did.</p> <p>18 Q. And this was published in 1999,</p> <p>19 correct?</p> <p>20 A. Yes.</p> <p>21 Q. Are you aware of any research</p> <p>22 or experimentation that Johnson & Johnson has</p> <p>23 done since 1999 to either -- to conclude that</p> <p>24 Ness and Cottreau regarding their opinion on</p> <p>25 inflammation and cancer is inaccurate?</p>

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<p style="text-align: right;">Page 198</p> <p>1 A. I'm not aware of any research, 2 again, that Johnson & Johnson has ever 3 performed on anything. 4 Q. Okay. Continuing along with 5 the theme of chronic cancer -- chronic 6 inflammation and ovarian cancer being 7 simplistic at all, I've now marked as Boyd 13 8 a paper by Trabert, T-r-a-b-e-r-t, et al., 9 titled "Prediagnostic Serum Levels of 10 Inflammation Markers and Risk of Ovarian 11 Cancer in the Prostate, Lung, Colorectal and 12 Ovarian Cancer, open paren, PLCO, close 13 paren, Screening Trial." 14 Did I read that correctly? 15 A. Yes. 16 Q. Okay. And if you see up above, 17 this is published in Gynecologic Oncology 18 2014, correct? 19 A. Yes. 20 Q. So we're moving forward from 21 2009. 22 Now, if you look at the list of 23 authors, you see that these individuals are 24 in various divisions, but they're all with 25 the National --</p>	<p style="text-align: right;">Page 200</p> <p>1 evidence implicates chronic inflammation as a 2 central mechanism in the pathogenesis of 3 ovarian cancer, the most lethal gynecologic 4 cancer among women in the United States. 5 Reference 1." 6 Did I read that correctly? 7 A. You did. 8 Q. And reference 1, I'll represent 9 to you, though by all means check, is the 10 Centers for Disease Control and Prevention 11 ovarian cancer statistics, 2010. 12 Did I read that correctly? 13 A. You did. 14 Q. So at this point right now 15 we're talking about researchers from NCI 16 quoting researchers from the CDC, correct? 17 A. Correct. 18 And I would add that my 19 inference from the use of this reference, 20 ovarian cancer statistics, is a reference to 21 support the beginning of this sentence that 22 the most lethal gynecologic cancer among 23 women is ovarian cancer in the United States. 24 That's the statistic to which they're 25 referring.</p>
<p style="text-align: right;">Page 199</p> <p>1 A. National Cancer Institute, yes. 2 I'm sorry. 3 Q. Okay. Do you know any of these 4 authors? 5 A. I may have met Mark Sherman 6 once, but, no, not really. 7 Q. Any reason to believe these 8 researchers with, one, the division of cancer 9 epidemiology and genetics, two, the HPV 10 immunology laboratory and the division of 11 cancer prevention within the National Cancer 12 Institute, are not respected researchers in 13 their respective fields? 14 A. I've already indicated that I 15 don't -- I look at the science that we're 16 discussing. I don't look at the researchers 17 who produced it and try to make a judgment as 18 to whether they're respected or not 19 respected, good people, bad people, 20 good-looking people, not good-looking people. 21 I prefer to discuss the science. 22 Q. Okay. Let's look at the very 23 first sentence on the next page under 24 Introduction. 25 And they write, "Epidemiologic</p>	<p style="text-align: right;">Page 201</p> <p>1 Reference 1 has nothing to do 2 with chronic inflammation as a central 3 mechanism in the pathogenesis of ovarian 4 cancer, I can assure you. 5 Q. And can you point out the CDC 6 document that states that the 7 epidemiologic -- 8 A. If you could produce the 9 document, I'd be happy to read it for you. 10 Q. You didn't pull that document 11 in preparation for writing your expert 12 report? 13 A. I think I actually pull this 14 document every year -- 15 Q. Okay. 16 A. -- because I think it's 17 important to be aware of cancer statistics 18 generally when you're writing review 19 articles. 20 Q. Do you have any objective 21 evidence which refutes the statement by these 22 NCI investigators that epidemiologic evidence 23 implicates chronic inflammation as a central 24 mechanism in the pathogenesis of ovarian 25 cancer?</p>

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<p>1 MS. MILLER: Objection.</p> <p>2 THE WITNESS: I think it's a</p> <p>3 hypothesis, and they haven't provided</p> <p>4 a citation to support the hypothesis.</p> <p>5 They've provided a citation to</p> <p>6 support the fact that epithelial</p> <p>7 ovarian cancer accounts for more</p> <p>8 deaths than all other gynecologic</p> <p>9 cancers combined, which is a fact.</p> <p>10 QUESTIONS BY MR. RESTAINO:</p> <p>11 Q. Doctor, are you guessing</p> <p>12 that's -- that that reference is limited to</p> <p>13 the most lethal gynecologic cancer --</p> <p>14 MS. MILLER: Objection.</p> <p>15 QUESTIONS BY MR. RESTAINO:</p> <p>16 Q. -- portion of their sentence?</p> <p>17 MS. MILLER: Objection. He</p> <p>18 asked to see it.</p> <p>19 THE WITNESS: Could you please</p> <p>20 repeat the question?</p> <p>21 QUESTIONS BY MR. RESTAINO:</p> <p>22 Q. Are you guessing that the</p> <p>23 reference to the CDC is only for the second</p> <p>24 half of that sentence?</p> <p>25 MS. MILLER: Objection.</p>	<p>1 division?</p> <p>2 A. Well, first of all, my</p> <p>3 understanding of this sentence is they're</p> <p>4 talking about cancer generally, and they're</p> <p>5 making some interesting hypotheses. And</p> <p>6 there are no citations to support any of the</p> <p>7 hypotheses in that sentence.</p> <p>8 Q. So does the lack of citations</p> <p>9 render a sentence unbelievable?</p> <p>10 A. No.</p> <p>11 MS. MILLER: Objection.</p> <p>12 Can you give me a second to</p> <p>13 object?</p> <p>14 THE WITNESS: It's not</p> <p>15 unbelievable. I just think that these</p> <p>16 are hypotheses that they're stating.</p> <p>17 I think they're trying to cover the</p> <p>18 waterfront in terms of all the</p> <p>19 hypotheses that have ever been</p> <p>20 rendered with respect to pathogenesis</p> <p>21 of ovarian cancer.</p> <p>22 QUESTIONS BY MR. RESTAINO:</p> <p>23 Q. And when you say "I think</p> <p>24 they're trying to cover the waterfront," are</p> <p>25 you speculating as to their intent in writing</p>
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<p>1 THE WITNESS: I'd like to see</p> <p>2 it, and we can confirm whether it is</p> <p>3 or not.</p> <p>4 QUESTIONS BY MR. RESTAINO:</p> <p>5 Q. Well, this paper with</p> <p>6 inflammation, ovarian and cancer twice in the</p> <p>7 title, did this paper come up during your</p> <p>8 review of the biomedical literature?</p> <p>9 A. Yes.</p> <p>10 Q. Did you review this article at</p> <p>11 that time?</p> <p>12 A. I read the abstract.</p> <p>13 Q. And -- okay. We'll leave it to</p> <p>14 that.</p> <p>15 The next sentence they write</p> <p>16 is, "Chronic inflammation can induce rapid</p> <p>17 cell division, increasing the possibility for</p> <p>18 replication error in effective DNA repair and</p> <p>19 subsequent mutation."</p> <p>20 Did I read that correctly?</p> <p>21 A. You did.</p> <p>22 Q. And do you have any objective</p> <p>23 evidence with which to contradict these NCI</p> <p>24 researchers when they stated in 2014 that</p> <p>25 chronic inflammation can induce rapid cell</p>	<p>1 this article?</p> <p>2 MS. MILLER: Objection.</p> <p>3 THE WITNESS: Yes.</p> <p>4 QUESTIONS BY MR. RESTAINO:</p> <p>5 Q. Okay. And, Doctor, do you have</p> <p>6 any objective evidence with which to</p> <p>7 contradict these NCI researchers when they</p> <p>8 state that "rapid cell division increases the</p> <p>9 possibility for replication error,</p> <p>10 ineffective DNA repair and subsequent</p> <p>11 mutation"?</p> <p>12 MS. MILLER: Objection.</p> <p>13 THE WITNESS: Again, that's</p> <p>14 producing negative data.</p> <p>15 No, it's impossible. I'm</p> <p>16 shaking my head, too.</p> <p>17 QUESTIONS BY MR. RESTAINO:</p> <p>18 Q. Yeah, there's a couple of times</p> <p>19 you said "generating negative data."</p> <p>20 If you do an experiment to test</p> <p>21 the effects of a drug on the treatment for</p> <p>22 ovarian cancer and the drug is an abject</p> <p>23 failure, that's negative data, isn't it?</p> <p>24 MS. MILLER: Objection.</p> <p>25 THE WITNESS: We're talking</p>

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<p style="text-align: right;">Page 206</p> <p>1 about two different things here. 2 QUESTIONS BY MR. RESTAINO: 3 Q. I'm not sure that we are. I'm 4 not sure you understand what negative means. 5 A. A negative result -- excuse me? 6 Please say that again? 7 Q. I'm not sure we are. I'm not 8 sure you understand what negative means in 9 this context. 10 A. I am pretty sure I do. 11 Q. Well, we're finding out, and so 12 far -- 13 A. You disagree with me. 14 Q. -- not looking good. 15 I'm sorry? 16 A. Who's not looking good? 17 Q. Okay. Let's go back to 1.3 18 times 1.3. 19 Doctor, is limited 20 replication -- 21 A. Let's go back to 1.3 times 1.3. 22 Q. Is limitless replicative 23 potential one of the hallmarks of cancer? 24 A. According to who? 25 Q. According to cancer</p>	<p style="text-align: right;">Page 208</p> <p>1 metastasis? 2 A. If you're going to go down the 3 list of the Hanahan Weinberg paper, it's 4 going to be the same answer. 5 Q. Sustained angiogenesis? 6 A. I've answered your question. 7 Q. I want to get it on the record, 8 sir. 9 Is that a hallmark of cancer? 10 MS. MILLER: Objection. It is 11 on the record because he answered your 12 question already. 13 THE WITNESS: You seem to be 14 reading from the list of hallmarks of 15 cancer as articulated by Hanahan and 16 Weinberg in 2011. And to the extent 17 that your intention it to continue 18 reading down the list, my answer is, I 19 believe that Hanahan and Weinberg 20 believe that these are hallmarks of 21 the cancer phenotype. 22 QUESTIONS BY MR. RESTAINO: 23 Q. Hanahan and Weinberg believe. 24 Do you know if it's generally 25 accepted in the scientific community that</p>
<p style="text-align: right;">Page 207</p> <p>1 specialists. 2 A. Show me what cancer specialists 3 you're talking about and where it's stated. 4 Q. Okay. Is self-sufficiency in 5 growth signaling a hallmark of cancer? 6 A. Are we getting back to Hanahan 7 and Weinberg? 8 Q. I'm just asking you about 9 hallmarks of cancer right now. 10 MS. MILLER: I guess it's been 11 asked and answered in that case. 12 THE WITNESS: I would agree 13 that Hanahan and Weinberg have written 14 a review article suggesting that the 15 last two phenotypic properties of 16 cancer cells are hallmarks of cancer 17 in their opinions. 18 QUESTIONS BY MR. RESTAINO: 19 Q. Is self-sufficiency in growth 20 signaling -- 21 A. Same answer. 22 Q. -- the hallmarks -- 23 A. If you're going to go down the 24 list, it's going to be the same answer. 25 Q. -- tissue invasion and</p>	<p style="text-align: right;">Page 209</p> <p>1 these are the hallmarks of cancer? 2 MS. MILLER: Objection. 3 THE WITNESS: I can't answer as 4 to what the scientific community 5 believes with respect to the Hanahan 6 and Weinberg paper. 7 QUESTIONS BY MR. RESTAINO: 8 Q. If we look at the Trabert 9 paper, in the next sentence, which is the 10 fourth line under Introduction, all the way 11 to the far right it starts with the word 12 "ovarian." 13 Do you see where I am, sir? 14 A. "Ovarian cancer has been 15 linked"? 16 Q. Yes. 17 A. Yes. 18 Q. "Ovarian cancer has been linked 19 to several events and conditions which are 20 related to inflammation and repair, including 21 incessant ovulation, endometriosis, exposure 22 to talc and asbestos, and in some studies, 23 pelvic inflammatory disease." 24 Did I read that correctly? 25 A. Yes.</p>

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<p style="text-align: right;">Page 210</p> <p>1 Q. And, Doctor, do you have any 2 objective evidence with which to contradict 3 these NCI researchers when they state that 4 "ovarian cancer has been linked to several 5 events and conditions which are related to 6 inflammation and repair"?</p> <p>7 MS. MILLER: I'm a little bit 8 lost. Where are you? What page?</p> <p>9 MR. RESTAINO: I'm on page 2 of 10 the Trabert paper under Introduction. 11 It's the fourth line of the first 12 paragraph.</p> <p>13 MS. MILLER: You read really 14 fast.</p> <p>15 THE WITNESS: I would suggest 16 that these are hypotheses. The 17 reference being cited is another 18 review article by these same authors 19 entitled "Possible Role of Ovarian 20 Epithelial Inflammation and Ovarian 21 Cancer."</p> <p>22 I do not consider a 23 self-reference of another review 24 article, the first word of which is 25 "possible," to be evidence that this</p>	<p style="text-align: right;">Page 212</p> <p>1 inflammatory disease." 2 Do you disagree that the 3 ovarian cancer has been linked to several 4 events and conditions which are related to 5 inflammation?</p> <p>6 MS. MILLER: Objection. 7 THE WITNESS: It depends. 8 QUESTIONS BY MR. RESTAINO: 9 Q. Upon? 10 A. What type of inflammation and 11 in what context. What type of ovarian 12 cancer.</p> <p>13 Q. Okay. Is there a difference in 14 your mind between the type of ovarian cancer 15 and whether it's associated with chronic 16 inflammation or not?</p> <p>17 A. I agree I -- let me correct 18 myself. My opinion generally is that it's 19 extraordinarily important to define which 20 type of the many types of ovarian cancer 21 we're discussing when we're hypothesizing 22 that one or another type of ovarian cancer 23 may be linked to one or another exposure or 24 physiologic condition. 25 Are you with me?</p>
<p style="text-align: right;">Page 211</p> <p>1 is, in fact, the case. 2 QUESTIONS BY MR. RESTAINO: 3 Q. Okay. Do you disagree with the 4 statement that "ovarian cancer has been 5 linked to several events and conditions which 6 are related to inflammation and repair"?</p> <p>7 MS. MILLER: Objection. 8 THE WITNESS: Well, you're 9 going to have to parse the 10 inflammation and repair. I'm assuming 11 you read it, and it's a poorly 12 constructed sentence. 13 What kind of repair, for 14 example?</p> <p>15 QUESTIONS BY MR. RESTAINO: 16 Q. The sentence above that we were 17 discussing, they are talking about 18 ineffective DNA repair, correct?</p> <p>19 A. They were. 20 Q. Okay. So now they state, 21 "Ovarian cancer has been linked to several 22 events and conditions which are related to 23 inflammation and repair, including incessant 24 ovulation, endometriosis, exposure to talc 25 and asbestos, and in some cases pelvic</p>	<p style="text-align: right;">Page 213</p> <p>1 Q. I'm with you. 2 Can you list for us today as 3 you sit here the different types of ovarian 4 cancer?</p> <p>5 A. Broadly speaking. 6 Q. Specifically speaking? 7 A. Well, that's an impossible 8 question to answer. 9 Are you talking about 10 histologic subtypes, or are you talking about 11 epithelial ovarian cancers versus sex cord 12 stromal tumors and germ cell tumors? I mean, 13 what --</p> <p>14 Q. Well, the first -- the last 15 ones you described are different forms of 16 histologic subtypes, correct? 17 So to make it easy for you, 18 whichever one you're -- 19 A. You don't need to make it easy 20 for me. I'm pretty familiar with the 21 subtypes of ovarian cancer. 22 Q. Okay. Which form of ovarian 23 cancer has not been linked to chronic 24 inflammation? 25 MS. MILLER: Objection.</p>

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<p style="text-align: right;">Page 214</p> <p>1 THE WITNESS: That's frankly a 2 ridiculous question. 3 (Boyd Exhibit 13 marked for 4 identification.) 5 QUESTIONS BY MR. RESTAINO: 6 Q. Is that so? Can I assume that 7 you can't answer that? 8 MS. MILLER: Objection. 9 THE WITNESS: I did answer. 10 QUESTIONS BY MR. RESTAINO: 11 Q. Do you know the answer to it? 12 MS. MILLER: Does this relate 13 to the pending question? 14 MR. RESTAINO: No, it's coming 15 next. 16 MS. MILLER: Okay. 17 THE WITNESS: I'm saying it's 18 impossible to answer a ridiculous 19 question, in my mind. 20 QUESTIONS BY MR. RESTAINO: 21 Q. Okay. Doctor, I've just marked 22 as Exhibit 14 and handed to you the 2000 23 paper by Hanahan and Weinberg that we've been 24 discussing, correct? 25 MS. MILLER: I'm confused. You</p>	<p style="text-align: right;">Page 216</p> <p>1 as they describe underneath there, the 2 acquired capabilities of cancer we've been 3 discussing; is that correct? 4 A. This is the list that you were 5 reciting, to the best of my knowledge. 6 And I should note further that 7 the caption to the figure reads, "We suggest 8 that most, if not all, cancers" -- and I 9 would insert the word "generally" there -- 10 "have acquired the same set of functional 11 capabilities during their development, albeit 12 through various mechanistic strategy." 13 So in other words, I believe 14 that they're talking about a suggestion in 15 this case that cancers generally have these 16 phenotypic properties, or display these 17 phenotypic properties. 18 Q. And now I suggest -- as you 19 suggested perhaps when you read Dr. Shih's 20 deposition transcript, I represented to him 21 how often this paper has been cited. And now 22 I'll represent to you, in the week or so 23 that's passed, this paper has been cited 24 30,148 times. 25 MS. MILLER: In one week?</p>
<p style="text-align: right;">Page 215</p> <p>1 didn't mark this earlier? You just 2 discussed it? 3 MR. RESTAINO: Yeah. 4 THE WITNESS: Well, this is the 5 first iteration of a paper by the same 6 title published in 2011, but you've 7 handed me a paper by Hanahan and 8 Weinberg published in 2000 called "The 9 Hallmarks of Cancer," yes. 10 QUESTIONS BY MR. RESTAINO: 11 Q. Okay. And if you turn to 12 page 2, there's a diagram with the hallmarks, 13 the acquired capabilities of cancer, as 14 listed by these authors on the bottom of it. 15 And that's what we've been 16 describing, correct? 17 A. I'm sorry, we're looking at 18 Figure 1 -- 19 Q. Yes, sir. 20 A. -- on page 2? 21 Q. Yes, sir. 22 A. And what's the question about 23 Figure 1? 24 Q. Oh, that's the diagram 25 representative of the hallmarks of cancer or,</p>	<p style="text-align: right;">Page 217</p> <p>1 MR. RESTAINO: In total. 2 MS. MILLER: Oh, you're saying 3 you're updating the number. 4 MR. RESTAINO: I'm updating the 5 number. 6 MS. MILLER: I thought you were 7 saying in one week. 8 QUESTIONS BY MR. RESTAINO: 9 Q. As you sit here today, are you 10 aware of any single medical paper that has 11 been referenced more than 30,148 times? 12 A. Well, not without spending more 13 time than we're going to allow to think about 14 it, no. 15 Q. I'll help you. 16 (Boyd Exhibit 14 marked for 17 identification.) 18 QUESTIONS BY MR. RESTAINO: 19 Q. I've now marked as Boyd 20 Exhibit 15 the 2000 publication by Hanahan -- 21 MS. MILLER: That was the 2000 22 publication. Do you mean -- 23 QUESTIONS BY MR. RESTAINO: 24 Q. -- the 2011 publication by 25 Hanahan and Weinberg titled "Hallmarks of</p>

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<p style="text-align: right;">Page 218</p> <p>1 Cancer: The Next Generation." And I'll 2 represent to you that this one has been cited 3 34,389 times as of last night. 4 Doctor, as a cancer researcher, 5 would you agree this is a very important 6 paper in the field of cancer? 7 A. I believe that it's been cited 8 a lot. 9 Q. Okay. Now, on page 2, they 10 have the illustration of the hallmarks of 11 cancer that they first published in 2000, 12 correct? 13 A. It's very similar, yes. 14 Q. Okay. And then on page 658 of 15 the paper, they have an updated diagram 16 there. 17 Do you see that, sir? 18 A. Yes. 19 Q. And on the top they have listed 20 emerging hallmarks, and below that enabling 21 characteristics. 22 Is that correct? 23 A. Yes. 24 Q. And see in the figure right, 25 the legend, the wording to the right of it,</p>	<p style="text-align: right;">Page 220</p> <p>1 all cancers generally and no cancer 2 specifically. 3 QUESTIONS BY MR. RESTAINO: 4 Q. Where are you getting the word 5 "hypothesis" from this when they state that 6 the hallmark is now "widely appreciated as 7 tumor-promoting consequences of an 8 inflammatory response"? 9 A. Because it strikes me as a 10 hypothetical statement without -- without 11 listing all of the known human cancers and 12 evidence that inflammation, et cetera, et 13 cetera, et cetera, is now widely appreciated 14 and so forth. 15 Widely appreciated by whom? 16 Q. As a cancer researcher, do you 17 have to understand the individual mechanisms 18 behind the development of each and every 19 different form of lung cancer that develops 20 in long-term smokers, i.e., non-small cell, 21 small cell, old cell? 22 In order to come to the 23 conclusion that smoking cigarettes causes 24 lung cancer, do you have to see the mechanism 25 for each and every individual one of those</p>
<p style="text-align: right;">Page 219</p> <p>1 if you go all the way down to the bottom, 2 there's one, two, three, four, five, six -- 3 seven lines up from the bottom starts off at 4 right with "inflammation." 5 Do you see that word, sir? 6 A. Yes. 7 Q. "Inflammation by innate immune 8 cells designed to fight infections and heal 9 wounds can instead result in their 10 inadvertent support of multiple hallmark 11 capabilities, thereby manifesting the now 12 widely appreciated tumor-promoting 13 consequences of inflammatory responses." 14 Did I read that correctly? 15 A. You did. 16 Q. And do you have any objective 17 evidence with which to contradict Hanahan and 18 Weinberg in this 2011 peer-reviewed, 19 published paper that the tumor-promoting 20 consequences of inflammatory responses is now 21 widely appreciated? 22 MS. MILLER: Objection. 23 THE WITNESS: Well, first, I 24 would suggest that this is a 25 hypothesis that is used to refer to</p>	<p style="text-align: right;">Page 221</p> <p>1 cancers? 2 MS. MILLER: Objection. 3 THE WITNESS: My impression is 4 that we're litigating ovarian cancer. 5 QUESTIONS BY MR. RESTAINO: 6 Q. But you've brought up several 7 times that authors appear to be relating 8 their information to cancer in general. So 9 my question goes back to that. Being 10 specific, we're talking about lung cancer and 11 smoking. 12 Does smoking cause lung cancer? 13 MS. MILLER: Objection. 14 THE WITNESS: Smoking can cause 15 lung cancer. And I would further add 16 that the epidemiologic association of 17 cigarette smoking with lung cancer is 18 so strong that it's possible to accept 19 that the association is real in terms 20 of causation. 21 QUESTIONS BY MR. RESTAINO: 22 Q. What is the epidemiologic 23 association of passive smoke inhalation and 24 lung cancer? 25 A. Do not know.</p>

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<p style="text-align: right;">Page 222</p> <p>1 Q. Would it surprise you to know 2 that it's 1.3? 3 A. No. 4 Q. If you turn to page 659 of 5 Hanahan and Weinberg, there's a first -- 6 there's a full paragraph on the right column 7 that starts "by 2000." 8 Do you see that, sir? 9 A. Yes. 10 Q. "By 2000, there are already 11 clues that the tumor-associated inflammatory 12 response had the unanticipated, paradoxical 13 effect of enhancing tumorigenesis and 14 progression, in effect helping incipient 15 neoplasias to acquire hallmark capabilities." 16 Did I read that correctly? 17 A. You did. 18 Q. Doctor, what is meant by 19 tumorigenesis? 20 A. The genesis of tumors. 21 Q. And how would you define tumor 22 regression? 23 A. It's a term that we don't 24 really use anymore. Initiation, promotion 25 and regression. They were useful decades</p>	<p style="text-align: right;">Page 224</p> <p>1 Q. You want to look at the 2 references? 3 A. Could we? 4 Q. Of course. 5 A. Yes. 6 Q. Okay. 7 A. These papers are referring to 8 existing cancers and either progression 9 and/or metastasis of existing cancers, not 10 the initiation of cancer, that is, the events 11 involved in -- the very early events involved 12 in the transformation process leading a 13 normal cell to become malignant and 14 ultimately metastatic. 15 So -- 16 Q. And in fact, Doctor, right 17 above the references they write, the last 18 four words, "have on neoplastic progression." 19 And that was the context of my question. 20 A. I think they're talking about 21 existing cancers. 22 Q. Yes. And progression of 23 existing cancer. 24 My only question was going to 25 be here, neoplastic progression, would you</p>
<p style="text-align: right;">Page 223</p> <p>1 ago, but we now like to refer to it a 2 multi-genetic, multi-step process. 3 Q. Has progression been absorbed 4 into that multi-genetic, multi-step process? 5 A. I think that's a fair 6 statement. 7 Q. Okay. The next sentence they 8 write here is, "In the ensuing decade, 9 research on the intersections between 10 inflammation and cancer pathogenesis has 11 blossomed producing abundant and compelling 12 demonstrations of the functionally important 13 tumor-promoting effects that immune cells, 14 hyphen, largely of the innate immune system, 15 hyphen, have on neoplastic progression." 16 Did I read that correctly? 17 A. You did. 18 Q. And there are four citations 19 there, correct? 20 A. Correct. 21 Q. And once again, here when they 22 write "neoplastic progression," would that be 23 something that you -- 24 A. Can we look at -- I'm sorry, go 25 ahead.</p>	<p style="text-align: right;">Page 225</p> <p>1 then encompass this term in the more modern 2 one that you were just sharing with us? 3 A. I would say that the entire 4 concept is irrelevant to the arguments that 5 we're having here today about whether talc 6 initiates ovarian tumorigenesis or not. 7 Q. Okay. Is it relevant to the 8 argument as to whether or not the plaintiff 9 experts' reliance upon chronic inflammation 10 is simplistic? 11 A. Couldn't follow your sentence. 12 Sorry. 13 Q. Okay. You stated earlier that 14 the opinions regarding chronic inflammation, 15 whether it was the plaintiff experts or 16 Dr. Saed, were -- and I can't paraphrase it 17 all, but the one word you used was 18 "simplistic," correct? You remember that? 19 A. Vaguely. 20 Q. And we've now gone through Ness 21 and Cottreau in 2009; Trabert, et al., in 22 2014; CDC in 2014. Now we're looking at 23 Hanahan 2011 talking about inflammation, and 24 not only initiation but also progression of 25 cancer. That's the only context I'm using</p>

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<p>1 this for.</p> <p>2 MS. MILLER: Is that a</p> <p>3 question?</p> <p>4 MR. RESTAINO: No, it was an</p> <p>5 explanation to why we were in this</p> <p>6 area.</p> <p>7 THE WITNESS: It sounded like a</p> <p>8 speech, but that's all right.</p> <p>9 QUESTIONS BY MR. RESTAINO:</p> <p>10 Q. It was just an explanation of</p> <p>11 why we're in this area.</p> <p>12 Let's go to the</p> <p>13 self-sufficiency in growth signals.</p> <p>14 As described by Hanahan --</p> <p>15 MS. MILLER: You got to slow</p> <p>16 down. Where are you?</p> <p>17 MR. RESTAINO: It's just one of</p> <p>18 the hallmarks. I'm just describing</p> <p>19 the term.</p> <p>20 MS. MILLER: What page? Where</p> <p>21 are you reading from?</p> <p>22 MR. RESTAINO: Well, any one of</p> <p>23 either the 2000 paper or the 2000 --</p> <p>24 THE WITNESS: But where in the</p> <p>25 paper, I think --</p>	<p>1 research paper, I will disagree with</p> <p>2 the doctor when you refer -- as to its</p> <p>3 implications in the medical</p> <p>4 literature.</p> <p>5 Secondly, I'm just asking in a</p> <p>6 general sense as to a cancer</p> <p>7 specialist --</p> <p>8 MS. MILLER: Okay. You just --</p> <p>9 you have the exhibit open. I'm</p> <p>10 confused. I didn't know if you were</p> <p>11 reading or asking a question.</p> <p>12 QUESTIONS BY MR. RESTAINO:</p> <p>13 Q. Doctor, generically speaking,</p> <p>14 is self-sufficiency in growth signals one of</p> <p>15 the hallmarks of any cancer?</p> <p>16 MS. MILLER: Objection.</p> <p>17 THE WITNESS: Where does it say</p> <p>18 self-sufficiency in growth signaling?</p> <p>19 MS. MILLER: I think he's</p> <p>20 saying that he's just asking this</p> <p>21 question unrelated to this document.</p> <p>22 I think. I'm confused as well.</p> <p>23 THE WITNESS: You'll have to</p> <p>24 explain your definition of</p> <p>25 self-sufficiency to me, please.</p>
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<p>1 MS. MILLER: We're on the 2011</p> <p>2 paper. That's my understanding.</p> <p>3 QUESTIONS BY MR. RESTAINO:</p> <p>4 Q. So go to the second column --</p> <p>5 or the second page.</p> <p>6 MS. MILLER: I think you don't</p> <p>7 realize you read very fast and you</p> <p>8 don't give page numbers, and I get</p> <p>9 very confused.</p> <p>10 MR. RESTAINO: But I wasn't</p> <p>11 reading from anything.</p> <p>12 MS. MILLER: You were reading</p> <p>13 from something. Nobody can talk that</p> <p>14 fast without reading.</p> <p>15 QUESTIONS BY MR. RESTAINO:</p> <p>16 Q. Doctor, sustaining</p> <p>17 proliferative signaling, can that lead to</p> <p>18 self-sufficiency in growth signals?</p> <p>19 MS. MILLER: I'm sorry, is this</p> <p>20 question based on this study or</p> <p>21 this -- sorry, it's not a study. It's</p> <p>22 a review article, I think you said?</p> <p>23 Is this question related to</p> <p>24 this exhibit?</p> <p>25 MR. RESTAINO: First of all, a</p>	<p>1 QUESTIONS BY MR. RESTAINO:</p> <p>2 Q. Could you pick up what is</p> <p>3 previously marked as Exhibit 14?</p> <p>4 A. Okay. We're back to 14. I'm</p> <p>5 sorry.</p> <p>6 Q. The 2000 paper, hallmarks of</p> <p>7 cancer.</p> <p>8 A. We're going back to 2000?</p> <p>9 Q. Yes.</p> <p>10 A. Okay.</p> <p>11 Q. Open to the second page.</p> <p>12 See the diagram, Figure 1?</p> <p>13 A. Yes.</p> <p>14 Q. You see the first acquired</p> <p>15 capability of cancer up at the top of it?</p> <p>16 A. Yes.</p> <p>17 Q. Is it titled "Self-Sufficiency</p> <p>18 in Growth Signals"?</p> <p>19 A. Yes, it was in 2000.</p> <p>20 And then in 2011 they changed</p> <p>21 the same phenotype to sustaining</p> <p>22 proliferative signaling.</p> <p>23 I would agree generally that</p> <p>24 sustained proliferative signaling is a</p> <p>25 hallmark of cancer, generally speaking.</p>

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<p style="text-align: right;">Page 230</p> <p>1 Q. Is it also a hallmark of 2 ovarian cancer? 3 A. Yes, generally speaking. 4 Q. Looking at the 2000 paper 5 again, the hallmark down below that, to the 6 right is "insensitivity to anti-growth 7 signals." 8 Is that a hallmark of cancer, 9 generally? 10 MS. MILLER: Objection. 11 THE WITNESS: Well, I would 12 simply agree with the authors that 13 suggest, "We suggest that most, if not 14 all, cancers have acquired the same 15 set of functional capabilities during 16 their development, albeit through very 17 mechanistic strategies." 18 I would agree with the 19 statement underneath the figure. 20 QUESTIONS BY MR. RESTAINO: 21 Q. Okay. Would you, as an expert 22 in ovarian cancer research, agree that 23 insensitivity to anti-growth signals occurs 24 in ovarian cancer also? 25 A. Yes. As I have previously</p>	<p style="text-align: right;">Page 232</p> <p>1 A. Yes, it's associated with, 2 again, mutational inactivation of the TP53 3 gene, which is extraordinarily common in 4 serous ovarian epithelial carcinomas and 5 indeed is the most frequently mutated tumor 6 suppressor gene in all cancers generally. 7 Q. Okay. All three of these will 8 lead to cellular proliferation, correct? 9 MS. MILLER: Objection. 10 All three of what? 11 QUESTIONS BY MR. RESTAINO: 12 Q. All three of these hallmarks 13 that we've just discussed. 14 MS. MILLER: Can you identify 15 which three you're referring to? 16 THE WITNESS: It's -- he's 17 referring to the top -- the three at 18 the top of Figure 1 in exhibit -- so 19 if we look at Figure 1 in Exhibit 14, 20 he's referring to the top three 21 phenotypic properties of acquired 22 capabilities of cancer. 23 QUESTIONS BY MR. RESTAINO: 24 Q. And the result of these three 25 hallmarks is going to be cellular</p>
<p style="text-align: right;">Page 231</p> <p>1 indicated, all cancers, including ovarian 2 cancers, are associated with the occurrence 3 and accumulation of mutations and oncogenes 4 and tumor suppressor genes. 5 The normal function of a tumor 6 suppressor gene is to inhibit growth, so in 7 other words, to provide an anti-growth 8 signal. And so when a tumor suppressor gene 9 such as TP53 or RB1 is inactivated, which 10 occurs frequently in ovarian cancer, then the 11 ovarian cancer cells become insensitive to 12 anti-growth signal. 13 Q. Okay. To the left of that 14 hallmark they write "evading apoptosis. " 15 Do you see that, sir? 16 A. Yes. 17 Q. And apoptosis is the death of 18 cells which occurs as a normal, controlled 19 part of an organism's growth and development; 20 would you agree? 21 A. It's generally referred to as 22 programmed cell death, but, yes. 23 Q. Fair enough. 24 Is evading apoptosis one of the 25 hallmarks, generally speaking, of cancer?</p>	<p style="text-align: right;">Page 233</p> <p>1 proliferation; would you agree? 2 A. Not necessarily, but would 3 certainly be more likely under these 4 circumstances than if these mutational events 5 leading to these phenotypic properties had 6 not occurred. 7 Q. Okay. 8 A. Tumor cells are not constantly 9 dividing. 10 Q. Let's turn to your expert 11 report, page 4. And you have a section 12 there, A, study design issues. The first one 13 is the use of DMSO as a solvent. 14 Did I read that correctly? 15 A. Yes. 16 Well, mostly correctly. 17 Q. Do you see the section "use of 18 DMSO as solvent"? 19 A. Yes. 20 Q. Okay. Colon. 21 And then you write in your 22 paragraph there -- if you look five lines 23 down, sir, towards the right, there's a 24 sentence where you start with, "But he 25 apparently paid."</p>

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<p style="text-align: right;">Page 234</p> <p>1 Do you see that?</p> <p>2 A. Yes.</p> <p>3 Q. "But he apparently paid no heed</p> <p>4 to recent research that has called into</p> <p>5 question whether the use of DMSO as a solvent</p> <p>6 can alter the effect of the treatment and</p> <p>7 skew the results."</p> <p>8 Reference 7 down below, Hall,</p> <p>9 MD, et al., "Say No to DMSO:</p> <p>10 Dimethylsulfoxide Inactivates Cisplatin,</p> <p>11 Carboplatin and Other Platinum Complexes."</p> <p>12 Did I read that correctly?</p> <p>13 A. You did.</p> <p>14 (Boyd Exhibit 16 marked for</p> <p>15 identification.)</p> <p>16 QUESTIONS BY MR. RESTAINO:</p> <p>17 Q. So I've marked as Boyd 16 your</p> <p>18 reference by Hall, et al. "Say no to DMSO."</p> <p>19 MS. MILLER: It's very catchy.</p> <p>20 MR. RESTAINO: It is. Easy to</p> <p>21 remember.</p> <p>22 QUESTIONS BY MR. RESTAINO:</p> <p>23 Q. Did I read that correctly, sir?</p> <p>24 Well, strike that.</p> <p>25 You recognize this paper,</p>	<p style="text-align: right;">Page 236</p> <p>1 typical in terms of a ligand receptor</p> <p>2 interaction such as epidermal growth factor,</p> <p>3 epidermal growth factor receptor being a</p> <p>4 ligand receptor interaction.</p> <p>5 So ligand actually has many</p> <p>6 definitions, depending on the context. The</p> <p>7 one you're using now is a chemical context,</p> <p>8 and I do not hold myself out as a chemist.</p> <p>9 Q. Okay. Do you agree that DMSO</p> <p>10 is a virtual, universal solvent?</p> <p>11 A. I believe that</p> <p>12 dimethylsulfoxide is used very commonly to</p> <p>13 dissolve chemicals of all kinds in an</p> <p>14 experimental context because many chemicals</p> <p>15 are readily soluble in DMSO.</p> <p>16 Q. So you're not disagreeing with</p> <p>17 Hall, et al., if they describe it as a</p> <p>18 virtual, universal solvent?</p> <p>19 A. I think that's a fair</p> <p>20 description of DMSO in this particular</p> <p>21 context.</p> <p>22 Q. Okay. Now, where I'm reading</p> <p>23 from, sir, is -- I'm not trying to play any</p> <p>24 word games from you -- is page 2, the middle</p> <p>25 paragraph under Introduction.</p>
<p style="text-align: right;">Page 235</p> <p>1 correct, sir?</p> <p>2 A. Yes.</p> <p>3 Q. Now, early on I asked you if</p> <p>4 you were an expert in pharmacology, and you</p> <p>5 said you were not, correct?</p> <p>6 A. Correct.</p> <p>7 Q. But do you have a basic</p> <p>8 understanding what the platinum-based drugs</p> <p>9 cisplatin, carboplatin and oxaliplatin are?</p> <p>10 A. Oxaliplatin.</p> <p>11 Q. That one, too.</p> <p>12 A. Yes.</p> <p>13 Q. Do you understand that they</p> <p>14 contain a ligand attached to them?</p> <p>15 A. Are you referring to platinum</p> <p>16 as a ligand?</p> <p>17 Q. Sir, do you know what a ligand</p> <p>18 is?</p> <p>19 A. It's -- I think what you're</p> <p>20 trying to get at is a ligand may generally be</p> <p>21 used as a definition for a molecule that</p> <p>22 interacts with another molecule.</p> <p>23 Earlier when we were discussing</p> <p>24 ligand, I was thinking of ligand in a cell</p> <p>25 biological context, which is much more</p>	<p style="text-align: right;">Page 237</p> <p>1 And all I can say is it's in</p> <p>2 the middle of the paragraph. The universal</p> <p>3 solvent language is there on the right-hand</p> <p>4 side about 11, maybe 12 lines down.</p> <p>5 A. Uh-huh.</p> <p>6 Q. Do you see that, sir?</p> <p>7 A. Yes.</p> <p>8 Q. And then a sentence ends with a</p> <p>9 reference 12, correct?</p> <p>10 A. Yes.</p> <p>11 Q. And then they write, "DMSO</p> <p>12 contains a nucleophilic sulfur, which allows</p> <p>13 it to coordinate with platinum complexes,</p> <p>14 displacing ligands and changing the structure</p> <p>15 of the complexes, open paren, 13 to 16. This</p> <p>16 renders platinum complexes unstable in DMSO."</p> <p>17 Did I read that correctly?</p> <p>18 A. I lost you, but I'll submit</p> <p>19 that you did.</p> <p>20 Q. Want me to read it again?</p> <p>21 A. No.</p> <p>22 Q. Or would you like to take a</p> <p>23 moment and read it yourself?</p> <p>24 A. No.</p> <p>25 Q. Okay. Now, is it your opinion</p>

60 (Pages 234 to 237)

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<p style="text-align: right;">Page 238</p> <p>1 that the nucleophilic sulfur which DMSO 2 contains interacts in any way whatsoever with 3 the mineral talc? 4 A. I'm sorry, I missed the first 5 part of the question. 6 Q. Is it your opinion that the 7 nucleophilic sulfur, which they describe 8 here, which DMSO contains, interacts in any 9 way whatsoever with the mineral talc? 10 A. I have no knowledge of the 11 interaction of DMSO with the mineral talc. 12 Q. Do you -- what objective 13 evidence do you have that shows that talcum 14 powder is rendered unstable in DMSO by this 15 nucleophilic sulfur? 16 A. None. 17 MS. MILLER: Objection. 18 THE WITNESS: Sorry. 19 MS. MILLER: Are we ready for a 20 break? 21 MR. RESTAINO: Ready for a 22 break? 23 MS. MILLER: I am. 24 THE WITNESS: Sure. 25 VIDEOGRAPHER: Off the record</p>	<p style="text-align: right;">Page 240</p> <p>1 MS. MILLER: It's starts on 2 3913, and what page do you want? 3 MR. RESTAINO: 3915. 4 MS. MILLER: So maybe we could 5 guess that it's around -- and we're 6 not supposed to guess today. 7 MR. RESTAINO: I know, but they 8 got page number -- well, let's see if 9 they have the page number up above. 10 THE WITNESS: Well, the problem 11 is this is the public access version 12 as opposed to the Cancer Research 13 version, and so the page numbers are 14 going to just be 1, 2, 3, 4 in the 15 public access version. 16 MS. MILLER: But if we guess, 17 13, 14, 15, it should be page 3. 18 What words are you looking for? 19 QUESTIONS BY MR. RESTAINO: 20 Q. "Discussion" is on the lower 21 right-hand side. 22 A. We can find the discussion 23 section if that's what we're doing. It's 24 going to be at the end. 25 Q. Yeah, I apologize. I actually</p>
<p style="text-align: right;">Page 239</p> <p>1 at 2:25 p.m. 2 (Off the record at 2:25 p.m.) 3 VIDEOGRAPHER: We are back on 4 the record at 2:38 p.m. 5 QUESTIONS BY MR. RESTAINO: 6 Q. Welcome back, Doctor. 7 Before we broke, we were 8 discussing the Hall paper which was your 9 reference. 10 Would you be kind enough, sir, 11 to turn to page -- to -- give me one second. 12 I apologize. I wrote down the wrong page 13 number. 14 Page 3919. And I apologize for 15 the delay. And -- 16 A. 39 -- in Hall, et al.? 17 Q. Yeah. 18 A. I'm sorry, I've got pages 1, 2, 19 3. 20 Q. And that's exactly what I'm 21 seeing also. 22 MS. MILLER: What's the issue? 23 What do you want? 24 THE WITNESS: It's just a page 25 number issue.</p>	<p style="text-align: right;">Page 241</p> <p>1 have two different versions. The printed 2 version and my electronic version are 3 different. My apologies. 4 A. All right. Discussion is 5 always at the end. 6 Q. It appears to be page 9. 7 A. Yes. 8 Q. Okay. Down below, Discussion. 9 "We have demonstrated here the profound 10 effects of DMSO on platinum drugs and 11 complexes that contain monodentate ligands." 12 Did I read that correctly? 13 A. You did. 14 Q. Does talc powder contain one of 15 those monodentate ligands? 16 A. I don't know. 17 Q. The bottom, last sentence of -- 18 in your expert report now on page 4, we were 19 discussing the use of DMSO as a solvent in A. 20 Do you see that, sir? 21 Sir, I'm on page 4. 22 A. "Dr. Saed's failure," et 23 cetera? 24 Q. Yes. "Dr. Saed's failure to 25 evaluate this possibility renders most of his</p>

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<p style="text-align: right;">Page 242</p> <p>1 results, open paren, those involving exposure 2 of cells to talc, close paren, unreliable." 3 Did I read that correctly? 4 A. Yes. 5 Q. And your one reference for this 6 entire paragraph is the Hall paper which has 7 to do with platinum-based metals and the 8 dissolution of the ligand by DMSO and has 9 nothing to do with talc; is that correct? 10 A. So far as I know. 11 I would add that over the 12 course of my career in conducting similar 13 studies, before having read this paper rather 14 recently and conducting studies with cells 15 and platinum, I, too, perform lots of 16 experiments, in fact, using DMSO as a solvent 17 for one or another compound that I was 18 treating cells with. 19 And I observed over the years 20 that after a period of time, even hours, a 21 clear solution containing a treatment 22 compound, if you will, or an experimental 23 compound, in DMSO frequently leads to the 24 clear solution turning brown over a short 25 period of time, which is consistent with the</p>	<p style="text-align: right;">Page 244</p> <p>1 QUESTIONS BY MR. RESTAINO: 2 Q. Inasmuch as the Hall paper 3 deals with metal-based, platinum-based 4 chemotherapy agents which are dissolved by 5 DMSO by losing the ligand, which has nothing 6 to do with talc, would you agree that your 7 opinion in this regard is unreliable, as you 8 describe Dr. Saed's opinion? 9 A. Well, first of all -- and I'm 10 just going to read the question. I'm sorry. 11 I believe earlier I suggested 12 that at least some of the elements that 13 constitute talc are, in fact, metals, e.g., 14 silica. So I don't think the whole 15 metal-based argument for why this is, out of 16 hand, irrelevant is valid. 17 I don't think the fact that 18 this is a chemotherapeutic agent has anything 19 to do with the argument. It just happens to 20 be a chemotherapeutic agent. It could be any 21 other chemical used to test any other 22 hypothesis about any other biological 23 phenomenon. 24 And so I think the essence of 25 your argument here, and I'm starting to lose</p>
<p style="text-align: right;">Page 243</p> <p>1 characterization of dimethylsulfoxide as a 2 chemical oxidant. 3 And just based on personal 4 experience, it was my inference from watching 5 experimental agents turn brown over a period 6 of hours, certainly days, and having to throw 7 out the solution and then start over again 8 with fresh DMSO and fresh chemical, that the 9 agent that I was testing was being chemically 10 modified. 11 Q. Okay. 12 A. It's a personal anecdote. 13 Q. Okay. And then in addition to 14 that, Doctor, inasmuch as the Hall paper 15 deals with metal-based, platinum-based 16 chemotherapy agents with ligands and CMSO 17 {sic}, is your failure to evaluate this paper 18 as it relates to the use of DMSO by Dr. Saed 19 render your opinions in this regard 20 unreliable? 21 MS. MILLER: Objection. 22 THE WITNESS: Sorry, I just 23 couldn't follow the sentence. 24 MS. MILLER: Yeah, I couldn't 25 either.</p>	<p style="text-align: right;">Page 245</p> <p>1 it because it's going up the screen, about 2 rendering my opinion -- 3 MS. MILLER: I can stop it. 4 THE WITNESS: -- about 5 rendering my opinion obsolete or 6 irrelevant is off target. 7 QUESTIONS BY MR. RESTAINO: 8 Q. Okay. Let's go down to the 9 bottom of page 4, determination of talc 10 dosage. And I'm sorry, page 4 of your expert 11 report. And we can put Hall to the side. 12 And is your opinion that 13 "Dr. Saed used a very highly concentrated 14 talc solution, hyphen, 500 milligrams of talc 15 per 10 milliliter of DMSO, with reference 8. 16 He then applied relatively enormous doses of 17 talc, hyphen, from 5 to 100 micrograms per 18 milliliter, directly to the treated cells." 19 Did I read that correctly? 20 A. Yes. 21 Q. 500 milligrams of talc per 22 10 milliliters, that's 50 milligrams per 23 milliliter, agreed? 24 A. Agree. 25 Q. Do you know what the usual and</p>

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<p style="text-align: right;">Page 246</p> <p>1 customary dissolution dose of talcum powder</p> <p>2 is when used for pleurodesis?</p> <p>3 A. It must be extraordinarily high</p> <p>4 based on the physiologic result that they're</p> <p>5 attempting to achieve --</p> <p>6 Q. How about --</p> <p>7 A. -- which is massive fibrosis in</p> <p>8 the closing off of the cavity between the</p> <p>9 chest wall and the lung.</p> <p>10 Q. Would it surprise you that it's</p> <p>11 5 grams dissolved in 50 to 100 millimeters of</p> <p>12 normal saline?</p> <p>13 A. It wouldn't surprise me at all.</p> <p>14 Q. And 5 grams equates to</p> <p>15 5,000 milligrams?</p> <p>16 A. I'm sorry, could we back up a</p> <p>17 minute? I would just like to be clear about</p> <p>18 what you were stating about the solvent</p> <p>19 that's used in pleurodesis. I believe you</p> <p>20 said normal saline.</p> <p>21 Q. Correct.</p> <p>22 NS. Does that make sense?</p> <p>23 A. Well, I'm reading normal</p> <p>24 saline.</p> <p>25 Q. Okay.</p>	<p style="text-align: right;">Page 248</p> <p>1 Dr. Saed's notebook where they actually</p> <p>2 played around with dissolving talc in a</p> <p>3 slurry at one point.</p> <p>4 Q. Play around --</p> <p>5 A. Freeze -- I'm sorry, that's an</p> <p>6 inappropriate term. I'm sure he's a serious</p> <p>7 man and doesn't play around in the lab.</p> <p>8 They -- they experimented with</p> <p>9 the process of dissolving talc in an aqueous</p> <p>10 solution as a slurry, and for reasons that</p> <p>11 aren't clear to me, as is the case for most</p> <p>12 of what goes on in his laboratory notebooks,</p> <p>13 they abandoned that approach and chose to use</p> <p>14 DMSO, which completely dissolved the talc.</p> <p>15 Q. And you don't know why they did</p> <p>16 that, though?</p> <p>17 A. Well, no, I can't -- I can't</p> <p>18 infer what they may have been thinking.</p> <p>19 Q. Do you know if the dose used by</p> <p>20 Dr. Saed is equivalent to the doses reported</p> <p>21 as used by others that have published,</p> <p>22 including, for example, Dr. Shukla,</p> <p>23 Dr. Akhtar twice?</p> <p>24 A. That's a good question. I did</p> <p>25 look at those papers, and I did look at the</p>
<p style="text-align: right;">Page 247</p> <p>1 A. But, no, I think it would have</p> <p>2 been fantastic.</p> <p>3 And I know you disagree with</p> <p>4 the retrospectoscope, but my whole point was</p> <p>5 we could avoided all of these -- could have</p> <p>6 avoided all of these uncertainties in this</p> <p>7 experimental design had he used an inert</p> <p>8 solvent such as normal saline to dissolve the</p> <p>9 talc.</p> <p>10 Q. Does talc dissolve in normal</p> <p>11 saline?</p> <p>12 A. Apparently in pleurodesis it</p> <p>13 seems to, based on what you just read.</p> <p>14 Q. So you don't know what is</p> <p>15 injected during pleurodesis?</p> <p>16 A. Talc.</p> <p>17 Q. Do you know what form, what --</p> <p>18 strike that.</p> <p>19 What -- do you know that it's a</p> <p>20 slurry that's involved?</p> <p>21 A. Yes.</p> <p>22 Q. Okay. Is a slurry different</p> <p>23 from normal saline?</p> <p>24 A. Yes.</p> <p>25 And I'm also familiar with</p>	<p style="text-align: right;">Page 249</p> <p>1 doses, and the dose range tended to be much</p> <p>2 lower in those papers.</p> <p>3 Q. Can you give us the dose range</p> <p>4 in those papers versus what Dr. Saed used?</p> <p>5 A. Roughly.</p> <p>6 MS. MILLER: Objection.</p> <p>7 THE WITNESS: Yeah, I'm not</p> <p>8 going to speculate without the papers</p> <p>9 in front of me. I'd be happy to read</p> <p>10 the doses from the X axis if you've</p> <p>11 got the papers on hand.</p> <p>12 QUESTIONS BY MR. RESTAINO:</p> <p>13 Q. Okay. Is it your opinion that</p> <p>14 there was a substantive difference in the</p> <p>15 doses --</p> <p>16 A. Absolutely.</p> <p>17 Q. -- used?</p> <p>18 And you're relying upon those</p> <p>19 papers and Dr. Saed's published paper for</p> <p>20 that?</p> <p>21 MS. MILLER: Objection.</p> <p>22 THE WITNESS: Well, I'm relying</p> <p>23 on more than that. That's part of the</p> <p>24 equation. Part of the calculus, if</p> <p>25 you will.</p>

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<p style="text-align: right;">Page 250</p> <p>1 QUESTIONS BY MR. RESTAINO: 2 Q. Okay. 3 A. I'm also relying on doses that 4 have been used in, for example, the Hamilton 5 study. 6 Q. Okay. 7 A. Where he injected approximately 8 10 milligrams into an entire rat ovary, which 9 compared -- which by my conservative estimate 10 is likely to contain tens of millions of 11 cells. And in this particular case, he's 12 treating 100-millimeter square dishes 13 containing a couple hundred thousand cells. 14 And the back-of-the-envelope 15 calculation is that he's using -- again, in 16 my estimation, using, granted, a subjective 17 term, a relatively massive dose. 18 Q. He's actually using -- when he 19 used the 5 micrograms per milliliter, he's 20 using 0.005 percent of that which is injected 21 during pleurodesis; is that correct? 22 MS. MILLER: Objection. 23 THE WITNESS: Well, I'll take 24 your arithmetic at face value. 25 I think it's important to</p>	<p style="text-align: right;">Page 252</p> <p>1 Q. Yes. 2 A. Correct. 3 Q. Okay. So when it's injected 4 there, it's going into a very small space to 5 begin with before it's distributed throughout 6 the pleural cavity, correct? 7 A. Yes, just as when one takes a 8 Pipetman and pipettes -- a certain amount of 9 DMSO containing talc onto a 100-millimeter 10 dish, and then swirling the dish around to 11 distribute the talc over the cells, it's a 12 similar concept. 13 Q. So in that -- what he's put 14 into his dish as compared to where that 15 needle goes, he's injected 0.0005 percent of 16 what's injected into a living human being? 17 A. Which is still a massive dose 18 based on the number of cells being treated, 19 relatively speaking. 20 You're trying to use arithmetic 21 to conflate the point I'm making. 22 Q. Okay. 23 A. And the number of cells that 24 are being treated and the space that's -- the 25 space that's receiving the amount of</p>
<p style="text-align: right;">Page 251</p> <p>1 consider the size of the pleural 2 cavity that is injected with talc 3 during the process of pleurodesis, 4 which as far as I can tell is used 5 primarily to prevent pleural effusions 6 or perhaps pneumothorax in patients 7 with lung cancer, by closing off what 8 is arguably a very large physical 9 space containing perhaps billions of 10 cells. 11 And Dr. Saed's experiments, 12 again, were performed in a 13 100-millimeter-squared petri dish, 14 which is roughly that large, with a 15 nonconfluent modulator of cells, 16 roughly 100,000, 200,000 perhaps. And 17 we're talking about logarithmic 18 differences of scale in terms of 19 pleurodesis versus the in vitro 20 experiments. 21 QUESTIONS BY MR. RESTAINO: 22 Q. When the pleurodesis is 23 injected, it's injected using a large bore, 24 typically an 18-gauge needle, correct? 25 A. An 18-gauge needle.</p>	<p style="text-align: right;">Page 253</p> <p>1 physiologic, biologic space that's receiving 2 the talc that's being either injected or 3 pipetted into a dish, injected into a human 4 or pipetted into a petri dish. 5 Q. Okay. Continue on with 6 determination of talc dose. You write, 7 second line from the bottom, "Indeed, the 8 evidence that any" -- and you bold "any" and 9 italicize "any" -- "talc can reach the 10 ovaries from external perineal use is weak." 11 Did I read that correctly? 12 A. You did. 13 Q. And are you an expert in the 14 migration of external particles from the 15 environment to the vagina to the fallopian 16 tubes and/or ovaries? 17 A. No. Sorry. 18 MS. MILLER: Objection. I -- 19 that was an objectionable question. 20 Please give me time to object. 21 THE WITNESS: So noted. 22 MS. MILLER: Don't rush. 23 QUESTIONS BY MR. RESTAINO: 24 Q. And you have a reference for 25 that, which is the 2010 IARC monograph on</p>

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<p>1 "Evaluation of carcinogenic risks to human, 2 Volume 93: Carbon black, titanium dioxide, 3 and talc 411," correct? 4 MS. MILLER: Objection. He has 5 three references, if I'm reading the 6 right footnote. 7 MR. RESTAINO: And I'm sorry, 8 I -- no, indeed, I'm reading from the 9 sentence, Jessica, "The evidence of 10 any talc can reach the ovaries from 11 external perineal use" -- 12 MS. MILLER: Are we looking at 13 footnote 10? Maybe I misunderstood 14 you, but it sounded like you were 15 saying there was one reference. 16 MR. RESTAINO: Oh, I'm just 17 reading the first one, the IARC one. 18 MS. MILLER: You said you have 19 a reference. 20 MR. RESTAINO: They're on the 21 same page. 22 QUESTIONS BY MR. RESTAINO: 23 Q. Do you see that, sir? 24 A. I do. 25 Q. And then turning to the next</p>	<p>1 capable of just saying "objection"? 2 You know that is the Federal 3 Rules, which is why we went to school 4 and we took all those classes. 5 MS. SHARKO: Okay. Let's just 6 move on. 7 (Boyd Exhibit 17 marked for 8 identification.) 9 QUESTIONS BY MR. RESTAINO: 10 Q. Doctor, I've now marked as Boyd 11 17 an article by McDonald, et al., or 12 McDonald, et al. And I'll represent to you 13 that this paper was published in March 2019. 14 Have you seen this paper 15 before? 16 A. I have. 17 Q. Okay. If you would turn to 18 page 12, if I'm correct, there should be a 19 section there in the upper left called 20 Discussion. 21 A. It's there. 22 Q. In the second paragraph they 23 write, "Talc, when applied to the perineum, 24 is believed to migrate to the upper genital 25 tract, passing through the open tract to the</p>
Page 255	Page 257
<p>1 page, you have a 1971 reference by Henderson, 2 et al., correct? 3 A. Correct. 4 Q. And then you have a 1996 5 reference by Heller, correct? 6 A. Correct. 7 Q. Have you seen any other papers 8 that have been published more recently 9 regarding migration of talc powder -- of 10 particles throughout the female reproductive 11 tract? 12 MS. MILLER: Objection. 13 Can you ask a better question 14 there? 15 Are you asking about talc 16 powders? Are you asking about 17 particles and -- 18 MR. RESTAINO: Talc powder and 19 particles. 20 MS. MILLER: Both? 21 MR. RESTAINO: Both. 22 MS. MILLER: Okay. That's a 23 new question. 24 MR. RESTAINO: Can't you just 25 say "objection"? Truly, are you</p>	<p>1 fallopian tubes and eventually reaching the 2 ovaries." References 11 and 16. 3 Did I read that correctly? 4 A. Yes, you did. 5 Can we dissect references 11 6 through 16? 7 Q. And I was going to suggest to 8 you, would you like to look at references 11 9 and 16? 10 A. Yes. 11 Q. Okay. Reference 11 is by 12 Cramer, et al., "The association between talc 13 use and ovarian cancer: A retrospective 14 case-control study in two US states," 15 published in Epidemiology in 2016; is that 16 correct? 17 A. You have read it correctly. 18 Q. And we discussed earlier 19 Dr. Daniel Cramer, the physician, 20 epidemiologist, correct? 21 A. And gynecologist, correct. 22 Q. And then reference 16 is the 23 Penninkilampi and Eslick paper, "Perineal 24 talc use and ovarian cancer: A systematic 25 review and meta-analysis," also published in</p>

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<p style="text-align: right;">Page 258</p> <p>1 Epidemiology. 2 This was in 2018; is that 3 correct? 4 A. I'm sorry, can we go back to 5 the original sentence? I believe you're 6 mixing references here. I'm sorry. 7 MS. MILLER: I'm afraid to 8 speak because you don't like me to say 9 anything more than objection, but -- 10 THE WITNESS: 11 and 16. 11 Henderson is 16, "Talc and carcinoma 12 of the ovary and cervix." 13 MR. RESTAINO: Oh, my mistake. 14 I'm sorry. 15 QUESTIONS BY MR. RESTAINO: 16 Q. And so reference 16 is the 17 Henderson study, correct? 18 A. Correct. 19 Q. Now, you reference the article, 20 the three references there, for the evidence 21 that talc can reach the ovaries from external 22 perineal use is weak; is that correct? 23 A. Well, if I recall, as I read 24 the articles, the first of the three 25 references that I cited I quote directly.</p>	<p style="text-align: right;">Page 260</p> <p>1 MR. RESTAINO: No. Just wonder 2 if he recalled reading that. 3 QUESTIONS BY MR. RESTAINO: 4 Q. Do you know what retrograde 5 transportation is as used with the female 6 reproductive tract? 7 A. I can infer that it would mean 8 stuff going north. 9 Q. Okay. And are you an expert -- 10 A. In stuff -- 11 Q. -- in the female reproductive 12 tract with stuff going north? 13 MS. MILLER: Objection. 14 THE WITNESS: No. 15 QUESTIONS BY MR. RESTAINO: 16 Q. Would you defer to a 17 gynecologist and a gynecologic oncologist 18 who -- for their -- their opinions on stuff 19 going north? 20 MS. MILLER: Objection. 21 THE WITNESS: I wouldn't 22 refer -- I'm sorry. I wouldn't defer 23 to people. I would defer to 24 literature and evidence. 25 MS. SHARKO: Ms. Thompson,</p>
<p style="text-align: right;">Page 259</p> <p>1 That is the IARC paper, or the monograph, if 2 you will, describing the evidence as weak, 3 and further animal studies showed no evidence 4 of retrograde transport of talc to the 5 ovaries. 6 And then we could further 7 dissect the actual data in the Henderson and 8 Heller papers, if you'd like, in terms of 9 what they actually found and whether it has 10 anything at all to do with talc getting from 11 the perineum to the ovaries. 12 Q. Do you recall in the -- your 13 review of the IARC monograph that they also 14 stated that in women with impaired clearance 15 function evidence of retrograde transport was 16 found? 17 A. No. 18 Q. Do you know -- 19 A. I remember what I wrote in my 20 footnote because it's there. 21 Q. Do you know -- 22 A. I don't remember anything in 23 the paper except what I've written here. 24 MS. MILLER: Do you want to 25 show him the papers?</p>	<p style="text-align: right;">Page 261</p> <p>1 didn't you say there was a no laughing 2 rule during depositions? 3 MS. THOMPSON: Well, Jessica is 4 laughing. She has been a good part of 5 the day. 6 MS. SHARKO: Not that I saw, 7 and I'm sitting right next to her. 8 MS. THOMPSON: And you'll have 9 to agree that things going -- stuff 10 going north is kind of funny, isn't 11 it, as a description? 12 That is all. It wasn't meant 13 to be derogatory in any way. 14 MR. RESTAINO: Can we move on? 15 MS. THOMPSON: Sorry, yes. 16 QUESTIONS BY MR. RESTAINO: 17 Q. Can we go to your expert report 18 at the top of page 5? And I apologize for 19 giggling. 20 A. No apology necessary. 21 Q. You write -- down toward the 22 bottom section of the top paragraph, you 23 start on the right, after reference 13, "But 24 the logical conclusion of this argument." 25 Do you see that, sir?</p>

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<p style="text-align: right;">Page 262</p> <p>1 A. Yes.</p> <p>2 Q. "But the logical conclusion of</p> <p>3 this argument would be that the same</p> <p>4 mechanisms of expulsion of talc from the</p> <p>5 areas of the female reproductive tract distal</p> <p>6 to the ovaries, open paren, vagina, cervix,</p> <p>7 uterus, fallopian tubes, close paren, should</p> <p>8 also prevent talc from otherwise migrating,</p> <p>9 hyphen, like a salmon upstream, hyphen,</p> <p>10 through this wash of bodily fluids,</p> <p>11 eventually reaching the ovaries."</p> <p>12 Is that correct?</p> <p>13 A. That's correct, and I apologize</p> <p>14 for using analogies that aren't entirely</p> <p>15 anatomical.</p> <p>16 Q. However, you don't have a</p> <p>17 reference for this opinion, correct?</p> <p>18 A. Well, if we could back up a</p> <p>19 little bit, I think it's useful to take this</p> <p>20 particular sentence in context.</p> <p>21 Q. In the context of the previous</p> <p>22 references?</p> <p>23 A. No, in the context of this</p> <p>24 entire paragraph.</p> <p>25 Q. Okay.</p>	<p style="text-align: right;">Page 264</p> <p>1 salmon upstream through the wash of bodily</p> <p>2 fluids."</p> <p>3 So in other words, it's got to</p> <p>4 be one way or the other. You can't argue</p> <p>5 that stuff is being constantly flushed out</p> <p>6 while suggesting that stuff is at the same</p> <p>7 time -- in other words, south and north at</p> <p>8 the same time through the same organ system.</p> <p>9 Q. Isn't it true that on a monthly</p> <p>10 basis when a woman is menstruating that the</p> <p>11 endometrium is sloughed off?</p> <p>12 A. It is true.</p> <p>13 Q. Is the internal aspect of the</p> <p>14 ovary sloughed off?</p> <p>15 A. What's the internal aspect of</p> <p>16 the ovary?</p> <p>17 Q. In any internal -- internal</p> <p>18 cellular components of the ovary, are they</p> <p>19 sloughed off during menstruation?</p> <p>20 MS. MILLER: Objection.</p> <p>21 THE WITNESS: You'd have to ask</p> <p>22 a more specific question than that.</p> <p>23 I'm sorry.</p> <p>24 QUESTIONS BY MR. RESTAINO:</p> <p>25 Q. Does -- during menstruation,</p>
<p style="text-align: right;">Page 263</p> <p>1 A. Could I read it?</p> <p>2 Q. Of course, sir.</p> <p>3 A. "In attempting to explain why</p> <p>4 talc would not produce inflammation and</p> <p>5 cancer in the intervening areas of the female</p> <p>6 reproductive anatomy, for example, Dr. Saed</p> <p>7 repeatedly referred to the wash,</p> <p>8 quote/unquote, of bodily fluids that would</p> <p>9 expel particulate matter," and then I</p> <p>10 referenced his deposition transcript.</p> <p>11 "Dr. Saed contrasted this protective</p> <p>12 mechanism to that of the ovaries, which he</p> <p>13 claims have no mechanism for removing foreign</p> <p>14 particles." Again, deposition transcript.</p> <p>15 "But the logical conclusion of</p> <p>16 this argument" -- and this is where I think</p> <p>17 context is important, so he's -- he's</p> <p>18 referring to the wash of bodily fluids that</p> <p>19 would expel particulate matter. "But the</p> <p>20 logical conclusion of this argument would be</p> <p>21 that the same mechanisms of expulsion of talc</p> <p>22 from areas of the female reproductive tract</p> <p>23 below the ovaries, i.e., vagina, cervix,</p> <p>24 uterus and fallopian tubes, should also</p> <p>25 prevent talc from otherwise migrating like a</p>	<p style="text-align: right;">Page 265</p> <p>1 does any part of the ovary, other than the</p> <p>2 egg that's bursting through, does any part</p> <p>3 of -- of the ovarian tissue slough off during</p> <p>4 menstruation?</p> <p>5 MS. MILLER: Objection.</p> <p>6 THE WITNESS: If you could ask</p> <p>7 a more specific question, I'd be happy</p> <p>8 to answer it.</p> <p>9 For example, what part of the</p> <p>10 ovary?</p> <p>11 QUESTIONS BY MR. RESTAINO:</p> <p>12 Q. Regarding the effect of</p> <p>13 menstruation on an ovary, on a monthly basis</p> <p>14 in a woman, would you defer to a</p> <p>15 gynecologist?</p> <p>16 A. Again, I generally don't defer</p> <p>17 to people or particular professions. I defer</p> <p>18 to textbooks and scientific literature to</p> <p>19 form opinions on anything that I'm rendering.</p> <p>20 Q. Okay. And do you render</p> <p>21 opinions on whether or not tissue is flushed</p> <p>22 from the ovary during menstruation?</p> <p>23 A. I'm not now because I just</p> <p>24 simply don't understand the question.</p> <p>25 Q. Okay. Are you familiar with</p>

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<p style="text-align: right;">Page 266</p> <p>1 any studies documenting that dead sperm and 2 inanimate sperm particles are efficiently 3 transported upward through the -- excuse me, 4 through the uterus and tubules? 5 MS. MILLER: Objection. 6 THE WITNESS: I'm familiar with 7 multiple allusions to 8 Dr. Clarke-Pearson's expert report 9 and/or deposition where this example 10 has been raised multiple times in 11 reading defendants' deposition 12 transcripts. So I assume that such 13 literature exists, but I've only read 14 it indirectly through plaintiffs' 15 attorneys' questions and defendants' 16 deposition transcripts. 17 QUESTIONS BY MR. RESTAINO: 18 Q. Of one, Dr. Clarke-Pearson. 19 That's the only one you've read? 20 MS. MILLER: Objection. That's 21 not what he said. 22 THE WITNESS: That's not what I 23 said. 24 QUESTIONS BY MR. RESTAINO: 25 Q. Well, regarding on the</p>	<p style="text-align: right;">Page 268</p> <p>1 transcripts of several defendant expert 2 witnesses versus the plaintiff expert 3 witnesses, is that a form of confirmation 4 bias? 5 MS. MILLER: Objection. 6 THE WITNESS: I think -- I'm 7 sorry for laughing, but that's an 8 unusually creative question. 9 I simply don't know how to 10 answer that. I'm sorry. 11 QUESTIONS BY MR. RESTAINO: 12 Q. Okay. Now, you've reviewed the 13 paper by Saed, et al., because Dr. Saed is 14 not the sole author of the paper "Molecular 15 Basis Supporting the Association with Talcum 16 Powder Use with Increased Risk of Ovarian 17 Cancer." Is that correct? 18 MS. MILLER: Objection. 19 THE WITNESS: Two things -- 20 noting objection. 21 First of all, it's Fletcher, et 22 al., and second -- 23 MS. MILLER: That was the 24 objection. 25 THE WITNESS: -- could we look</p>
<p style="text-align: right;">Page 267</p> <p>1 plaintiff side, what other plaintiff 2 gynecological oncology deposition did you 3 read? 4 MS. MILLER: Huh? Objection. 5 THE WITNESS: I read -- 6 MS. MILLER: Wait a minute. 7 Objection. 8 You don't want me to say 9 anything further, but he never said 10 anything about reading Dr. -- I think 11 you just need to read his testimony 12 and ask your question again. 13 QUESTIONS BY MR. RESTAINO: 14 Q. Doctor, did you read Clarke -- 15 Dr. Clarke-Pearson's expert report and his 16 deposition transcript? 17 A. I skimmed it. I've read much 18 more carefully the deposition transcripts of 19 several defendants' expert witnesses where 20 they are consistently asked on multiple 21 occasions by plaintiffs' lawyers as to 22 whether they're familiar with 23 Dr. Clarke-Pearson's testimony that dead 24 sperm can migrate north. 25 Q. So in reading the deposition</p>	<p style="text-align: right;">Page 269</p> <p>1 at the paper? 2 QUESTIONS BY MR. RESTAINO: 3 Q. Yes. And I've marked the paper 4 as 18. 5 A. Are we done with McDonald? 6 Q. With who? 7 A. McDonald? 8 Q. Yes, sir. 9 A. Thank you. 10 (Boyd Exhibit 18 marked for 11 identification.) 12 QUESTIONS BY MR. RESTAINO: 13 Q. So what we've been as calling 14 Dr. Saed's paper, or Fletcher, et al., does 15 have multiple coauthors, correct? 16 A. Does indeed. 17 Q. And do you know any of these 18 authors? 19 A. No. 20 Q. And the paper itself was 21 submitted -- originally submitted to 22 Gynecologic Oncology, correct? 23 A. It's my understanding. 24 Q. And there were two peer 25 reviewers that took a look at it, or at least</p>

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<p style="text-align: right;">Page 270</p> <p>1 two that we know of?</p> <p>2 A. The latter. For the record,</p> <p>3 there were at least two that rendered an</p> <p>4 opinion, yes.</p> <p>5 Q. Okay. And would you agree that</p> <p>6 in the typical peer-review process of a</p> <p>7 medical or scientific paper, reviewers with</p> <p>8 expertise in the subjective -- in the subject</p> <p>9 matter of the submitted manuscript are</p> <p>10 selected to conduct a review?</p> <p>11 A. That's certainly the goal. It</p> <p>12 doesn't always happen, but that's -- that's</p> <p>13 clearly the goal of peer review.</p> <p>14 Q. Okay.</p> <p>15 A. Obviously with millions of</p> <p>16 papers being published and a finite number of</p> <p>17 journals, the expertise and the content don't</p> <p>18 always tick and tie, but that's certainly the</p> <p>19 goal of peer review, yes.</p> <p>20 Q. Is it reasonable to conclude</p> <p>21 that the two peer reviewers for Gynecologic</p> <p>22 Oncology were experts in the subject matter</p> <p>23 of the Fletcher, et al., paper?</p> <p>24 MS. MILLER: Objection. Calls</p> <p>25 for speculation.</p>	<p style="text-align: right;">Page 272</p> <p>1 you recall that.</p> <p>2 A. Well, that's an interesting</p> <p>3 question on several accounts. Yes, I did</p> <p>4 read it, but I'd like to have the opportunity</p> <p>5 to comment on the content of the entire</p> <p>6 letter as opposed to some sentences extracted</p> <p>7 out of context, perhaps.</p> <p>8 Q. Okay.</p> <p>9 A. So if we could share the</p> <p>10 letter, that would be very useful.</p> <p>11 Q. I will do that.</p> <p>12 A. Thank you.</p> <p>13 Q. Have you ever had a paper</p> <p>14 submitted to a journal and have it rejected?</p> <p>15 A. Many times.</p> <p>16 Q. So the papers that you've</p> <p>17 had -- that you've submitted that have been</p> <p>18 rejected many times, were they flawed papers?</p> <p>19 A. That's a very vague term,</p> <p>20 "subjective."</p> <p>21 Q. Were they papers that were</p> <p>22 subsequently published by another journal?</p> <p>23 A. I would say, again, there's a</p> <p>24 fine line between guessing and estimating.</p> <p>25 First, let's start with the</p>
<p style="text-align: right;">Page 271</p> <p>1 THE WITNESS: I have no idea</p> <p>2 what the expertise of the anonymous</p> <p>3 reviewers of the Fletcher, et al.,</p> <p>4 paper submitted to Gynecologic</p> <p>5 Oncology is -- are.</p> <p>6 I'm sorry. I'm losing track of</p> <p>7 my own sentence.</p> <p>8 QUESTIONS BY MR. RESTAINO:</p> <p>9 Q. Did you read the letter from</p> <p>10 the editor of Gynecologic Oncology to</p> <p>11 Dr. Saed regarding that the journal,</p> <p>12 Gynecologic Oncology, was currently only</p> <p>13 accepting less than 20 percent of the</p> <p>14 manuscripts submitted?</p> <p>15 A. I did.</p> <p>16 And could we have a copy of the</p> <p>17 letter if we're going to discuss the letter?</p> <p>18 Q. If we're going to discuss the</p> <p>19 letter, sure.</p> <p>20 A. Sounds like we are. I'm</p> <p>21 just -- I'm sorry.</p> <p>22 Q. Yeah, I think we're just coming</p> <p>23 to it. I'm not going to get into the details</p> <p>24 of it. I just want to know at this point if</p> <p>25 you've read it and you've reviewed that, if</p>	<p style="text-align: right;">Page 273</p> <p>1 reality of publishing papers.</p> <p>2 In my 35-year experience of</p> <p>3 publishing papers and indeed serving as a</p> <p>4 peer reviewer for more than 40, 45 journals,</p> <p>5 and indeed with respect to Gynecologic</p> <p>6 Oncology in particular, having reviewed,</p> <p>7 conservatively, 150 papers for Gynecologic</p> <p>8 Oncology, having served on the editorial</p> <p>9 board of Gynecologic Oncology, and indeed</p> <p>10 having served as associate editor for</p> <p>11 Gynecologic Oncology, I can assure you that</p> <p>12 there are very few papers in science</p> <p>13 generally, and biomedical science generally,</p> <p>14 in the context of any journal that are</p> <p>15 accepted without revision on first</p> <p>16 submission.</p> <p>17 And so it's -- it's not only</p> <p>18 usual, it is in fact the norm, for a paper to</p> <p>19 receive constructive -- generally always</p> <p>20 constructive -- comments about how the paper</p> <p>21 could be improved based on the opinions of</p> <p>22 the presumptive expert reviewers.</p> <p>23 Q. And it's true, is it not, that</p> <p>24 Fletcher, et al., then submitted the paper to</p> <p>25 Reproductive Sciences?</p>

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<p>1 A. After they were disinvited to 2 submit a revised version to Gynecologic 3 Oncology, correct. 4 Q. Disinvited? 5 A. Yeah, again, could we see the 6 letter, please, so we don't have to guess 7 about what's boilerplate and what's actually 8 not boilerplate on a letter from the editor 9 from Gynecologic Oncology? 10 I've got quite a lot of 11 experience with the journal. 12 (Boyd Exhibit 19 marked for 13 identification.) 14 QUESTIONS BY MR. RESTAINO: 15 Q. I'll mark this as 19. 16 And this is what you've seen, 17 sir? 18 A. Yes. 19 Q. And the first page, you see 20 it's to Ghassan Saed with cc's, correct? 21 A. Yes. 22 Q. From Gynecologic Oncology, 23 correct? 24 A. Correct. 25 Q. And you see the first</p>	<p>1 says exactly the same thing, I can assure 2 you. It's a fact. 3 Q. Does that decrease the merit of 4 what they're saying in the letter? 5 A. No, I'm just helping you to 6 understand the letter. You're interested in 7 discussing the letter. 8 Q. Well, I understand letters from 9 editors and peer-reviewers, very much so. 10 A. Well, we're talking about a 11 specific letter from a specific journal in 12 this case, Gynecologic Oncology, and I'm not 13 sure if you're familiar with Gynecologic 14 Oncology or not. 15 Q. And while I've never submitted 16 a paper to this journal, can you sit there 17 and tell us today that this first paragraph 18 is the exact same paragraph that they send to 19 every paper that they don't accept, the 20 80 percent of which is submitted to them? 21 Can you sit here and say that 22 that paragraph is the exact same thing? 23 A. That are rejected outright; in 24 other words, on first submission, I can state 25 that as a fact.</p>
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<p>1 paragraph: "Your paper, referenced above, 2 has now been reviewed by at least two experts 3 in the field and the editors. Based on the 4 reviewers' comments, we must inform you that 5 while your work is not without merit, we are 6 unable to accept your manuscript for 7 publication in Gynecologic Oncology. In the 8 last year, we have seen a significant 9 increase in the number of manuscripts 10 submitted to the journal and as a result, we 11 are now accepting less than 20 percent of the 12 manuscripts submitted to Gynecologic 13 Oncology." 14 Did I read that carefully? 15 A. I don't know, but you read it 16 correctly. 17 Q. I read it correctly? 18 A. Yes. 19 Q. Where in there does it say he 20 was disinvited? 21 A. We haven't gotten there yet. 22 First of all, the paragraph 23 that you just read, for any paper that's 24 rejected outright from Gynecologic Oncology, 25 this is boilerplate. Every single letter</p>	<p>1 Q. Okay. Now, do you know if this 2 paper was ultimately submitted to 3 Reproductive Sciences? 4 A. I'd like to move on with this 5 letter. I mean, you're -- to use a phrase 6 I've used -- cherry-picking pieces of the 7 letter and avoiding others that I think bear 8 on the veracity of the paper as the reviewer 9 saw it submitted to Gynecologic Oncology. 10 Q. I'm actually going to come back 11 to that, so I'd like to -- 12 A. Well, I hope so, because I 13 think it's important. 14 Q. Well, your attorney is going to 15 have a chance to ask you about it, as I said. 16 Okay? It's my turn -- 17 A. Well, you said you were going 18 to come back to it, but -- 19 Q. I may if we have time. Okay. 20 MS. MILLER: Again -- 21 THE WITNESS: For the record, 22 I'd like to continue on the topic of 23 this particular paper from this 24 particular journal because I think it 25 bears on the quality of the manuscript</p>

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<p style="text-align: right;">Page 278</p> <p>1 as the reviewers from Gynecologic 2 Oncology viewed it. 3 MR. RESTAINO: And if we have 4 time, I'm going to get back to it. I 5 have more questions about that letter. 6 THE WITNESS: Noted. 7 MS. MILLER: Are we done with 8 this exhibit? 9 MR. RESTAINO: Just for the 10 time being. I'm going to return to 11 it. 12 QUESTIONS BY MR. RESTAINO: 13 Q. Now, on the bottom of page 6 of 14 your expert report, you have a section 15 Inadequate Control Experiments. 16 Do you see that, sir? 17 A. Yes. 18 Q. And you write, "Dr. Saed's 19 studies do not adequately address his 20 hypothesis that there is a biological 21 mechanism linking exposure to talc, open 22 paren, a hydrated magnesium silicate compound 23 consisting of magnesium, silicon and oxygen, 24 hyphen, all of which are found at one or 25 another concentration in the human body and</p>	<p style="text-align: right;">Page 280</p> <p>1 case and research -- 2 MS. MILLER: I'm sorry. 3 THE WITNESS: It's quite all 4 right. 5 My point was that the talc 6 particle is generally considered to be 7 chemically inert, and I was perhaps 8 opining at length about inert stuff in 9 the body that constitutes talc. 10 But my point here, as I 11 intended it then and as I intend it 12 today, is that talc is an inert -- a 13 chemically inert particle and that 14 it's my opinion, as apparently it was 15 for the other investigators that we've 16 discussed most recently that perform 17 similar experiments in vitro treating 18 cells with talc and so forth, to use 19 other inert particles to control for 20 the effect -- the simple effect of 21 placing extraordinarily large amounts 22 of inert particles on cells in culture 23 in order to measure a biological 24 phenomenon. 25 So in other words, is it</p>
<p style="text-align: right;">Page 279</p> <p>1 are, in fact, considered, quote, essential 2 elements, close paren, to ovarian 3 carcinogenesis because Dr. Saed failed to 4 perform additional control experiments 5 designed to test whether other particulate 6 compounds, such as, for example, cornstarch, 7 open paren, a powdered carbohydrate derived 8 from the endosperm of corn kernels, close 9 paren, or a particulate compound more 10 chemically similar to talc, such as finely 11 ground beach sand, open paren, silicon 12 dioxide, close paren, produce the same 13 results." 14 Did I read that correctly? 15 A. I'll submit that you did. 16 Q. Okay. Now, when you say 17 that -- why in this paragraph did you add 18 that magnesium silicon and oxygen are 19 considered essential elements? 20 A. I honestly don't remember. 21 Q. Okay. 22 A. My point is I think that -- if 23 I recall when I was composing this probably 24 late at night, since that's when I did 25 essentially all of my work related to this</p>	<p style="text-align: right;">Page 281</p> <p>1 specific to talc or is it simply the 2 result of dumping a lot of powder 3 on -- or finely ground, you know, 4 titanium oxide or glass beads, for 5 example, I think one of the 6 investigators used. I think they were 7 a little more careful in their 8 scientific approach, which I think 9 speaks to Dr. Saed's thought process 10 in designing the appropriate control 11 experiments for the ones he described 12 in this paper. 13 QUESTIONS BY MR. RESTAINO: 14 Q. Hydrogen is an essential 15 element also, isn't it? 16 A. Yes. 17 Q. Because it was left out of your 18 essential elements here. 19 A. Again, I think I explained my 20 rationale for describing them as essential 21 elements, and that's certainly not the -- the 22 gist nor the crux of my -- of my criticism of 23 the experimental design. 24 Q. Wasn't your intent to indicate 25 to any reader of this paragraph that these</p>

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<p>1 elements, including magnesium, silicon, 2 oxygen and the left out hydrogen, are 3 essentially safe because they're essential 4 elements in our body? 5 A. It was my point to indicate 6 that talc is inert, chemically unreactive, 7 generally speaking. And I apologize if it 8 doesn't meet your standards for describing a 9 compound as chemically inert. 10 Q. Is it physiologically inert? 11 A. I believe it is. 12 Q. And what do you base that upon? 13 A. Chemically inert is 14 physiologically inert. I mean -- 15 Q. Okay. 16 A. -- the cells, the tissues of 17 the human body, is -- of the human body is -- 18 are you about to hand us something? 19 Q. Yes, sir. 20 MS. MILLER: Finish your 21 sentence. If you're done. 22 THE WITNESS: Chemically inert, 23 in my mind, suggests that a compound, 24 a chemical, does not spontaneously 25 react with anything, which of course</p>	<p>1 I just want to look at them with you. 2 And you've got magnesium there, 3 correct? 4 MS. MILLER: Objection. 5 What is this? 6 MR. RESTAINO: Chemical 7 structure. 8 THE WITNESS: Could we 9 stipulate -- 10 MS. MILLER: Is this a 11 chemistry test? 12 THE WITNESS: Could we 13 stipulate that we've got magnesium, 14 silicon, oxygen and hydrogen here and 15 both agree? 16 QUESTIONS BY MR. RESTAINO: 17 Q. Yes. 18 And would you agree that all 19 the essential elements that we have been 20 discussing are located in that compound? 21 A. Yes. 22 Q. Okay. The bottom of page 6 and 23 top of page 7 of your expert report. 24 After you've been discussing 25 various additional control experiments and</p>
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<p>1 would include anything that you 2 classify as physiological. 3 QUESTIONS BY MR. RESTAINO: 4 Q. Are hydrated magnesium 5 silicates inert? 6 A. Well, there are different forms 7 of hydrated magnesium silicates, I presume, 8 which is where you're going with this, and 9 I'm sure some of them aren't -- a good 10 example would be the difference between -- 11 let's make something up -- water, H₂O, which 12 is oxygen and hydrogen, and hydrogen 13 peroxide, H₂O₂, which differ by a single 14 oxygen molecule, one being very inert, the 15 other being very reactive. 16 So I think it's very safe to 17 say even though I don't hold myself out as a 18 chemist, that there are very likely to be 19 other hydrated magnesium silicates that are 20 not inert. 21 (Boyd Exhibit 20 marked for 22 identification.) 23 QUESTIONS BY MR. RESTAINO: 24 Q. I've marked as Exhibit 20 25 "Chemical Structure of Essential Elements."</p>	<p>1 experiments of Dr. Saed, et al., could have 2 performed, you write, "Such experiments 3 testing the potential biological effects of 4 other particulate compounds like talc could 5 have been used to determine whether his 6 findings were driven by some quality that is 7 unique to talc or rather its particulate form 8 generally, the characteristics of which are 9 shared by many other compounds." 10 Did I read that correctly? 11 A. You did, and I opined on that 12 point extensively just literally a few 13 seconds ago. 14 Q. Yes. 15 Do you know if those 16 experiments are being planned by Dr. Saed? 17 A. How would I know what he's 18 planning to do? 19 Q. Well, you're criticizing saying 20 that he could have done a lot of other 21 studies, that he could have done in vivo 22 studies, that he could have done a lot more, 23 which is not the normal sequence of 24 scientific study. 25 But all I'm asking now is, do</p>

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<p style="text-align: right;">Page 286</p> <p>1 you know if he's doing those experiments as</p> <p>2 we sit here today?</p> <p>3 MS. MILLER: Objection.</p> <p>4 THE WITNESS: Is that a</p> <p>5 rhetorical question, sir?</p> <p>6 QUESTIONS BY MR. RESTAINO:</p> <p>7 Q. No. I'm just asking, do you</p> <p>8 know?</p> <p>9 A. I haven't spoken to Dr. Saed --</p> <p>10 Q. Okay.</p> <p>11 A. -- so I have no way of knowing</p> <p>12 what he's planning to do in the future.</p> <p>13 Q. But you've criticized him for</p> <p>14 not correlating his in vitro studies with</p> <p>15 some in vivo studies at this time, correct?</p> <p>16 MS. MILLER: Objection.</p> <p>17 THE WITNESS: I'm criticizing</p> <p>18 him for his studies, his laboratory</p> <p>19 notebook, his deposition, his expert</p> <p>20 report, all the things that I've seen.</p> <p>21 Obviously I can't criticize him</p> <p>22 for things that he may or may not do</p> <p>23 in the future. I think that's kind</p> <p>24 of, again, I'm sorry, a silly</p> <p>25 question.</p>	<p style="text-align: right;">Page 288</p> <p>1 study.</p> <p>2 A. So we're switching gears here</p> <p>3 and going from a ostensible carcinogenesis</p> <p>4 study to a therapeutic study?</p> <p>5 Q. Yes.</p> <p>6 A. Okay?</p> <p>7 Q. Yes.</p> <p>8 A. Please proceed.</p> <p>9 Q. Is that fair, the sequence I</p> <p>10 mentioned, in vitro to in vivo/animal to</p> <p>11 phase I, phase II, phase III, maybe phase IV?</p> <p>12 A. Yeah --</p> <p>13 MS. MILLER: Objection.</p> <p>14 THE WITNESS: -- I just wanted</p> <p>15 to understand --</p> <p>16 MS. MILLER: Dr. Boyd, please</p> <p>17 give me time to object.</p> <p>18 THE WITNESS: I just wanted to</p> <p>19 wrap my head around the massive</p> <p>20 context which -- we were talking about</p> <p>21 carcinogenicity, and now we're talking</p> <p>22 about therapeutic.</p> <p>23 So understanding that there's</p> <p>24 been a massive context switch in terms</p> <p>25 of the question that you're asking,</p>
<p style="text-align: right;">Page 287</p> <p>1 QUESTIONS BY MR. RESTAINO:</p> <p>2 Q. Doctor, isn't it true that in</p> <p>3 scientific research it's not uncommon,</p> <p>4 especially when looking at treatment</p> <p>5 modalities, to go from an in vitro cellular</p> <p>6 petri dish study, and if the results are</p> <p>7 promising, to move on to an in vivo study or</p> <p>8 an animal study, and if the results are</p> <p>9 promising, to move on to a phase I clinical</p> <p>10 trial, phase II, phase III, and in some cases</p> <p>11 phase IV?</p> <p>12 MS. MILLER: Objection.</p> <p>13 QUESTIONS BY MR. RESTAINO:</p> <p>14 Q. Would you agree that's normal</p> <p>15 sequence of some scientific study?</p> <p>16 MS. MILLER: Objection to those</p> <p>17 questions.</p> <p>18 THE WITNESS: To what kind of</p> <p>19 scientific study? Are we talking</p> <p>20 about treatment studies or toxicology,</p> <p>21 carcinogenicity studies?</p> <p>22 QUESTIONS BY MR. RESTAINO:</p> <p>23 Q. I actually started by saying,</p> <p>24 when looking at treatment study modalities,</p> <p>25 treatment study. Let's use a treatment</p>	<p style="text-align: right;">Page 289</p> <p>1 could you please ask the question</p> <p>2 again?</p> <p>3 QUESTIONS BY MR. RESTAINO:</p> <p>4 Q. You really need for me to</p> <p>5 repeat that, what normal study is for looking</p> <p>6 at the treatment modalities for any drug?</p> <p>7 In vitro goes on to in vivo,</p> <p>8 which might include animal, which might</p> <p>9 include phase I where you look at safety,</p> <p>10 phase II where we look at safety and dose,</p> <p>11 phase III where we're looking at effect,</p> <p>12 phase IV we're looking at -- for the</p> <p>13 production or any adverse events.</p> <p>14 Do you really need that</p> <p>15 repeated again?</p> <p>16 MS. MILLER: Objection.</p> <p>17 Is that your question?</p> <p>18 THE WITNESS: I'm --</p> <p>19 MS. MILLER: I would like to</p> <p>20 object to your tone, and if your</p> <p>21 question is "do you really need that</p> <p>22 repeated again," I'm going to object</p> <p>23 as argumentative.</p> <p>24 THE WITNESS: I actually didn't</p> <p>25 hear a word you said because you sound</p>

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<p>1 extremely angry and you're yelling at</p> <p>2 me, and I frankly don't appreciate it.</p> <p>3 QUESTIONS BY MR. RESTAINO:</p> <p>4 Q. You're a scientist, correct?</p> <p>5 Is that what you do for a</p> <p>6 living?</p> <p>7 A. Actually, I spend most of my</p> <p>8 time as an administrator and as an executive</p> <p>9 at this point in my career.</p> <p>10 Q. What percentage of your time</p> <p>11 today is spent in administrative versus</p> <p>12 research?</p> <p>13 A. 90 percent.</p> <p>14 Q. Okay. Have you ever been</p> <p>15 involved in testing for a potential treatment</p> <p>16 of any condition?</p> <p>17 A. That's an extraordinarily vague</p> <p>18 question.</p> <p>19 In what context?</p> <p>20 Q. Let's say a drug treatment for</p> <p>21 ovarian cancer.</p> <p>22 Have you ever been involved</p> <p>23 in -- in the experiment looking at whether a</p> <p>24 particular compound could be an effective</p> <p>25 treatment of ovarian cancer? Ever been</p>	<p>1 A. I agree that preclinical</p> <p>2 studies are generally required for novel</p> <p>3 compounds to get to a human phase I,</p> <p>4 phase II, phase III and so forth studies,</p> <p>5 yes.</p> <p>6 Q. Would you criticize any</p> <p>7 researcher who was conducting an in vitro</p> <p>8 study, who at the same time was also not</p> <p>9 testing that compound in an animal model at</p> <p>10 the same time?</p> <p>11 A. I would if that investigator</p> <p>12 titled a paper, based on those in vitro</p> <p>13 studies in a tissue culture dish, "Molecular</p> <p>14 basis supporting the association of talcum</p> <p>15 powder use with increased risk of ovarian</p> <p>16 cancer." He's a long way from ovarian</p> <p>17 cancer, sir.</p> <p>18 Q. Okay. You can agree the next</p> <p>19 step for any type of study like that -- but</p> <p>20 now we're back to cancer, because you've made</p> <p>21 a monumental change. We're back to the risk.</p> <p>22 Would you agree that the next</p> <p>23 step is in vivo?</p> <p>24 A. No. I disagree that I've made</p> <p>25 a monumental change. We've always been on</p>
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<p>1 involved with that?</p> <p>2 A. Are you done?</p> <p>3 Q. Yes, sir.</p> <p>4 A. Well, as I mentioned earlier, I</p> <p>5 served on the committee for experimental</p> <p>6 medicine of the gynecologic oncology group</p> <p>7 for 17 years, and so I would offer to you</p> <p>8 that it's a fair statement that I haven't</p> <p>9 been -- I have been involved in the design of</p> <p>10 studies, the purpose of which was to develop</p> <p>11 clinical trials in ovarian cancer.</p> <p>12 Q. And when you've been involved</p> <p>13 in the design of these trials, or of these</p> <p>14 studies, at what level? The in vitro level,</p> <p>15 the in vivo or animal level, phase I,</p> <p>16 phase II, phase III or all of them?</p> <p>17 A. All of them.</p> <p>18 Q. Is it your understanding then</p> <p>19 in that -- in that situation that the normal</p> <p>20 sequence is to go in vitro, and if the</p> <p>21 results are positive, to move on to in vivo,</p> <p>22 which might be animal, and then to move on to</p> <p>23 phase I to phase II, phase III, maybe</p> <p>24 phase IV?</p> <p>25 Is that the normal sequence?</p>	<p>1 cancer.</p> <p>2 Q. But I switched to the treatment</p> <p>3 thing, and you criticized that as being a</p> <p>4 monumental change.</p> <p>5 So we're back to now risk and</p> <p>6 cancer.</p> <p>7 A. We've always been on cancer.</p> <p>8 Q. Okay.</p> <p>9 A. You switched from</p> <p>10 carcinogenicity to therapeutics in cancer.</p> <p>11 We've never shifted off cancer.</p> <p>12 Q. Well, by definition we just</p> <p>13 did. So I've changed the channel back to</p> <p>14 cancer.</p> <p>15 A. I disagree.</p> <p>16 Q. Now looking in the cancer risk</p> <p>17 area, is it normal science to conduct an in</p> <p>18 vitro study contemporaneously with an animal</p> <p>19 study?</p> <p>20 MS. MILLER: Objection.</p> <p>21 THE WITNESS: I've never</p> <p>22 performed such a contemporaneous</p> <p>23 study, no.</p> <p>24 QUESTIONS BY MR. RESTAINO:</p> <p>25 Q. If you take a look at your</p>

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<p style="text-align: right;">Page 294</p> <p>1 expert report now at the bottom of page 8, 2 and you've got a section there on CA125 3 findings, correct? 4 A. Correct. 5 Q. CA125 stand for cancer antigen 6 125? 7 A. Yes. 8 Q. And the last sentence on 9 page 8, going on to the next page, you state, 10 "The FDA-approved use of measuring serum 11 CA-125 levels is in the context of a bio -- 12 quote, biomarker, end quote, to monitor 13 response to ovarian cancer treatment. 14 Reference 28," which is Saed report at 18, 15 along with citing Jelovac D and Armstrong, 16 correct? 17 A. Correct. 18 Q. Would you agree that CA125 is 19 the most extensively studied biomarker for 20 use in the early detection of ovarian cancer? 21 MS. MILLER: Objection. 22 THE WITNESS: It's the only 23 putative biomarker for ovarian cancer; 24 thus, it would by definition be the 25 most extensively studied.</p>	<p style="text-align: right;">Page 296</p> <p>1 A. I think we've established that. 2 Q. Have you ever published on 3 CA125 since your 2000 publication, current 4 understanding of the epidemiology, clinical 5 implications of BRCA1, BRCA2 mutations for 6 ovarian cancer? 7 A. Well, there are a lot of 8 questions there. I'm not sure what BRCA1 and 9 BRCA2 have to do -- oh, I see. I published a 10 paper on whether -- yeah, now I've got it. 11 Okay. So other than that paper 12 where I believe the hypothesis was that CA125 13 levels may differ in BRCA1 and BRCA2-linked 14 ovarian cancers from matched ovarian cancers 15 not associated with BRCA1 or 2 mutations -- I 16 think that's the paper you're referring to. 17 Q. Okay. 18 A. I have, in fact, coauthored a 19 paper related to CA125 insofar as I chaired a 20 conference at the Banbury Center at the Cold 21 Spring Harbor Laboratory, the purpose of 22 which was to bring multiple content experts 23 together and dissect the UKCTOCS clinical 24 trial, which, of course, involved -- well, I 25 can explain the trial to you, but I'll stop</p>
<p style="text-align: right;">Page 295</p> <p>1 QUESTIONS BY MR. RESTAINO: 2 Q. The next sentence you write, 3 "Although such measurements have also been 4 tested experimentally for decades in an 5 effort to detect ovarian cancer at an early 6 age, the specificity and sensitivity of serum 7 CA125 levels in this context are unacceptably 8 low, and the assay is neither useful nor 9 approved for this purpose. Reference 29." 10 Did I read that correctly? 11 A. No, you said "age" instead of 12 "stage," but I'll give you that mistake. 13 Q. And your reference 29 says, 14 "See above reference to UKCTOCS clinical 15 trial"; is that correct? 16 A. Yes, we refer to it as the 17 UKCTOCS trial. United Kingdom Collaborative 18 Trial of Ovarian Cancer Screening is what the 19 acronym stands for. 20 Q. Okay. 21 A. I hope you heard my answer. 22 Q. I did, and I'm reading it also. 23 Do you order CA125 blood tests? 24 A. No. I'm not an oncologist. 25 Q. Okay.</p>	<p style="text-align: right;">Page 297</p> <p>1 there. The answer is yes. 2 Q. Okay. Now, regarding the 3 sensitivity being unacceptably low and the 4 assay has been neither useful nor approved 5 for this purpose, approved by whom? 6 A. The FDA. 7 Q. And it's your expert opinion as 8 you sit here that CA125 has not been approved 9 for use with detecting ovarian cancer? 10 A. That's not what I said. 11 Would you like me to read what 12 I said? 13 Q. I think the report itself will 14 stand on itself. 15 A. Well, you misstated my report, 16 sir. 17 Q. Well, go ahead so the record is 18 clear, sir. 19 A. The FDA-approved use of 20 measuring CA125 levels is in the context of a 21 biomarker to monitor response to treatment 22 and, I might add, recurrence, where it is 23 extremely effective. 24 Q. Okay. 25 A. It's not effective in any way,</p>

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<p style="text-align: right;">Page 298</p> <p>1 shape or form in the early detection or</p> <p>2 diagnosis of ovarian cancer, the context in</p> <p>3 which it's not FDA approved.</p> <p>4 Q. So it's your opinion it's not</p> <p>5 effective in any way, shape or form in the</p> <p>6 early detection or diagnosis of ovarian</p> <p>7 cancer; is that correct?</p> <p>8 A. Yes.</p> <p>9 Q. Okay. And now you have a</p> <p>10 reference here, your reference 30 of</p> <p>11 Scholler N and Urban N, CA125 in ovarian</p> <p>12 cancer, correct? That's your reference 30?</p> <p>13 A. I do see the reference 30 at</p> <p>14 the bottom of the page. I'd like to look to</p> <p>15 see what I am referencing it for. "Increased</p> <p>16 serum CA125 levels have been reported in</p> <p>17 benign conditions such as..."</p> <p>18 My point here is that the</p> <p>19 reason it's not FDA approved for the early</p> <p>20 detection or diagnosis of ovarian cancer are</p> <p>21 multifactorial, one being the sensitivity and</p> <p>22 specificity for ovarian cancer is</p> <p>23 extraordinarily low because increased serum</p> <p>24 levels of CA125, as I write here in reference</p> <p>25 Scholler and Urban, have been reported in,</p>	<p style="text-align: right;">Page 300</p> <p>1 Nicole Urban. And you can see down at the</p> <p>2 bottom, this is published in 2015 -- or at</p> <p>3 the top, Gynecologic Oncology 2015.</p> <p>4 When you were preparing for</p> <p>5 your expert report and evaluating CA125, did</p> <p>6 you see this paper?</p> <p>7 A. I didn't need to see it because</p> <p>8 I was already aware of it.</p> <p>9 Q. Okay. And if you could turn to</p> <p>10 the second page, bottom paragraph of the left</p> <p>11 column?</p> <p>12 A. Yes. A review?</p> <p>13 Q. It's above materials and</p> <p>14 methods on the second page, left column, five</p> <p>15 lines up.</p> <p>16 A. One, two, three --</p> <p>17 Q. Starts with "CA125" on the</p> <p>18 right-hand side. "CA125 is a predictive."</p> <p>19 Do you see that?</p> <p>20 A. Yes.</p> <p>21 Q. "CA125 is a predictive marker</p> <p>22 for EOC that becomes increasingly sensitive</p> <p>23 with proximity to diagnosis, reference 16."</p> <p>24 Do you have any objective</p> <p>25 evidence to contradict Urban, et al., in 2015</p>
<p style="text-align: right;">Page 299</p> <p>1 and I quote, benign conditions such as</p> <p>2 endometriosis, pregnancy, ovulation, liver</p> <p>3 diseases, congestive heart disease and</p> <p>4 infectious diseases, and so forth and so on.</p> <p>5 The other reason, perhaps</p> <p>6 unstated, is that if we presume for the</p> <p>7 moment that epithelial ovarian cancer is one</p> <p>8 disease, which it's not, but if we -- for the</p> <p>9 purposes of early diagnosis of the cancer,</p> <p>10 which we -- cancers which we lump together as</p> <p>11 epithelial ovarian carcinoma, only</p> <p>12 approximately half of all patients at the</p> <p>13 time of diagnosis of epithelial ovarian</p> <p>14 carcinoma have an elevated serum CA125; hence</p> <p>15 its lack of utility in early detection as</p> <p>16 well as its lack of specificity.</p> <p>17 (Boyd Exhibit 21 marked for</p> <p>18 identification.)</p> <p>19 QUESTIONS BY MR. RESTAINO:</p> <p>20 Q. Okay. Well, let's look at a</p> <p>21 more current publication by Nicole Urban.</p> <p>22 You reference Scholler and</p> <p>23 Urban, 2007. Here's "Identifying</p> <p>24 postmenopausal women at elevated risk for</p> <p>25 epithelial ovarian cancer." Lead author is</p>	<p style="text-align: right;">Page 301</p> <p>1 when they say "CA125 is a predictive marker</p> <p>2 for EOC that becomes increasing sensitive</p> <p>3 with proximity to diagnosis"?</p> <p>4 A. I'm not aware that this is in</p> <p>5 fact the case, and, you know, I -- it's hard</p> <p>6 to understand the context without having read</p> <p>7 a paper entitled "Assessing Lead Time," "lead</p> <p>8 time" typically being associated with the</p> <p>9 term "bias."</p> <p>10 Q. You testified that you're aware</p> <p>11 of this paper, correct?</p> <p>12 A. Yes, I'm aware of this paper.</p> <p>13 Q. And you reference --</p> <p>14 A. Where you're pulling the</p> <p>15 sentence out of one of many sentences in the</p> <p>16 paper and asking me to opine on a particular</p> <p>17 sentence.</p> <p>18 Q. Yeah, many sentences which have</p> <p>19 absolutely nothing to do with specificity and</p> <p>20 sensitivity and early detection of ovarian</p> <p>21 cancer, I'll give you that. I'm trying to</p> <p>22 stay on point of what you said.</p> <p>23 Now, look at the final sentence</p> <p>24 of that paragraph there, and they say, "Both</p> <p>25 CA125 and HE4 show promise as risk and early</p>

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<p style="text-align: right;">Page 302</p> <p>1 detection markers," again with a number of</p> <p>2 references, 16 and then 20 through 23. Five</p> <p>3 references, correct?</p> <p>4 MS. MILLER: You read that</p> <p>5 wrong.</p> <p>6 QUESTIONS BY MR. RESTAINO:</p> <p>7 Q. I'll read it again.</p> <p>8 "Both CA125 and HE4 show</p> <p>9 promise as risk and early detection markers."</p> <p>10 Did I read that correctly?</p> <p>11 A. You did.</p> <p>12 Q. Okay. Now, near the end of the</p> <p>13 paragraph of CA125, page 9 of your report --</p> <p>14 so we're on page 9, that top paragraph. Six</p> <p>15 lines up on the right-hand side, you write,</p> <p>16 "Because increased CA -- CA/125" --</p> <p>17 Do you see that, sir?</p> <p>18 A. Yes.</p> <p>19 Q. -- "expression can reflect any</p> <p>20 number of causes, physiologic states, or</p> <p>21 conditions other than ovarian cancer, its use</p> <p>22 as a detection tool is highly disfavored and</p> <p>23 is considered ineffective from a clinical</p> <p>24 perspective."</p> <p>25 I've read that correctly?</p>	<p style="text-align: right;">Page 304</p> <p>1 another article. This one's titled "Role of</p> <p>2 CA125 in predicting ovarian cancer survival -</p> <p>3 a review of the epidemiological literature"</p> <p>4 by Gupta, et al., published 2009 in the</p> <p>5 Journal of Ovarian Research.</p> <p>6 And 2009 is after the 2007</p> <p>7 paper by Scholler and Urban which you</p> <p>8 referenced, correct, sir?</p> <p>9 A. I'll submit that whatever you</p> <p>10 said is correct.</p> <p>11 Q. Okay. And if you look on the</p> <p>12 left -- on the second page, left column, you</p> <p>13 have a heading "CA125 in ovarian cancer."</p> <p>14 Do you see that, sir?</p> <p>15 A. Yes.</p> <p>16 Q. And they state here, "The most</p> <p>17 widely used tumor marker in ovarian cancer,</p> <p>18 often considered the gold standard, is CA125,</p> <p>19 reference 19."</p> <p>20 Did I read that correctly?</p> <p>21 A. You did.</p> <p>22 Q. And the reference 19 is by</p> <p>23 Hogdall, E, titled "Cancer antigen 125 and</p> <p>24 prognosis."</p> <p>25 Did you see that?</p>
<p style="text-align: right;">Page 303</p> <p>1 A. You did.</p> <p>2 Q. And you have the professional</p> <p>3 ability to use CA125 from a clinical</p> <p>4 perspective?</p> <p>5 MS. MILLER: Objection.</p> <p>6 THE WITNESS: No.</p> <p>7 QUESTIONS BY MR. RESTAINO:</p> <p>8 Q. And do you -- and you don't</p> <p>9 have any references for that statement</p> <p>10 either, do you?</p> <p>11 A. It's just a follow-on to the</p> <p>12 entire paragraph above it where I've provided</p> <p>13 references.</p> <p>14 And furthermore, if you're</p> <p>15 attempting to equate that sentence you read</p> <p>16 in my expert report with a hypothetical</p> <p>17 statement about two biomarkers together</p> <p>18 showing promise, I think it's an inaccurate</p> <p>19 comparison.</p> <p>20 Q. Okay.</p> <p>21 A. Apples meet oranges.</p> <p>22 (Boyd Exhibit 22 marked for</p> <p>23 identification.)</p> <p>24 QUESTIONS BY MR. RESTAINO:</p> <p>25 Q. I've just marked as Exhibit 22</p>	<p style="text-align: right;">Page 305</p> <p>1 A. I did.</p> <p>2 Q. And that was published in 2008?</p> <p>3 A. Right.</p> <p>4 Q. Also after Scholler and Urban,</p> <p>5 correct?</p> <p>6 A. Right.</p> <p>7 Q. Would you agree that CA125 is</p> <p>8 the most widely tumor marker in ovarian</p> <p>9 cancer?</p> <p>10 A. It's the only tumor marker used</p> <p>11 in ovarian cancer in a clinical context;</p> <p>12 thus, it's the most widely used.</p> <p>13 Q. Okay. Which --</p> <p>14 MS. MILLER: Let him finish,</p> <p>15 please.</p> <p>16 Please finish your answer.</p> <p>17 THE WITNESS: You know, it's</p> <p>18 late. Perhaps we could get beyond</p> <p>19 rhetorical questions and get to more</p> <p>20 substantive questions related to CA125</p> <p>21 and the pathogenesis of ovarian</p> <p>22 cancer, which is what Dr. Saed is</p> <p>23 attempting to suggest based on his</p> <p>24 work.</p> <p>25</p>

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<p style="text-align: right;">Page 306</p> <p>1 QUESTIONS BY MR. RESTAINO: 2 Q. Okay. 3 A. This all has to do, as you can 4 see from the title on relevance, the 5 relevance -- the possible relevance of CA125 6 in predicting the survival. It has nothing 7 to do with the tumorigenesis. 8 Q. Does it have anything to do 9 with tumor progression? 10 A. It has to do with survival from 11 advanced ovarian cancer. 12 Q. Okay. If you look at the same 13 paragraph we were just looking at in the 14 Gupta study, page 2, left column, all the way 15 down at the bottom, second to last -- four 16 lines up, they write, "In addition, elevated 17 levels of CA125 are more strongly associated 18 with serous, rather than mucinous, tumors," 19 with reference 25. 20 Did I read that correctly? 21 A. You did. 22 Q. Okay. And do you agree with 23 that statement? 24 A. I would probably just say "so 25 what" with respect to Dr. Saed's work and his</p>	<p style="text-align: right;">Page 308</p> <p>1 autoantibodies, open paren, AAb, close paren, 2 that may have diagnostic capacity for 3 invasive epithelial ovarian cancer, with AABs 4 to p53 proteins and cancer-tested antigens, 5 open paren, CTAGs, as prominent examples." 6 Did I read that correctly? 7 A. You did. 8 Q. Okay. And on the third page in 9 the left column, at the bottom they have 10 materials and case methods. 11 Do you see that, sir? 12 A. Yes, I do. 13 And I have to respectfully 14 suggest that after we get through reading 15 sentences throughout this paper, that I'm 16 probably going to have ask you to -- to form 17 a coherent question related to all of these 18 comments that you're currently reading and 19 asking me if you're reading them correctly 20 throughout the paper. 21 Q. Okay. If you look at the 22 materials and methods, you see that this is 23 a -- we conducted a case-control study nested 24 within the EPIC cohort, hyphen, in a 25 population-based, multi-center prospective</p>
<p style="text-align: right;">Page 307</p> <p>1 suggestion that CA125 is somehow involved in 2 the transformation of a normal ovarian 3 epithelial cell into a malignant one. 4 (Boyd Exhibit 23 marked for 5 identification.) 6 QUESTIONS BY MR. RESTAINO: 7 Q. Okay. I'd like to show you now 8 a paper I've marked as Exhibit 23 by lead 9 author Kaaks, K-a-a-k-s, et al. And this is 10 titled "Tumor-associated autoantibodies as 11 early detection markers for ovarian cancer, 12 question mark, a prospective evaluation." 13 And this was published in the 14 International Journal of Cancer in 2018; is 15 that correct? 16 A. Let's assume you are correct. 17 I'll stipulate, yes. 18 Q. And if you look at the final 19 author line on the left, do you see there's 20 Daniel W. Cramer again, correct? 21 A. Correct. 22 Q. First sentence of the abstract, 23 which is on -- actually on page 2, they 24 write, "Immune-proteomic screening has 25 identified several tumor-associated</p>	<p style="text-align: right;">Page 309</p> <p>1 cohort study in ten European countries, 2 hyphen, further extension of an earlier study 3 on CA125 and other early detection markers 4 for ovarian cancer." Two references, 4 and 5 5. 6 Did I read that correctly? 7 A. You did. 8 Q. If you go back to the second 9 page where we have the abstract, et al., they 10 have a section there, What's New? 11 Do you see that, sir? 12 A. I do. 13 Q. And -- you know, I'm not going 14 to ask that because you've answered that 15 already, so let's strike that. I'll move on. 16 And you've mentioned the UK 17 Collaborative Trial of Ovarian Cancer 18 Screening, UKCTOCS? 19 Did you pronounce that acronym? 20 A. UKCTOCS is how we refer to it, 21 yes. 22 Q. UKCTOCS? 23 A. Uh-huh. 24 Q. Can I use that also? 25 A. Sure.</p>

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<p style="text-align: right;">Page 310</p> <p>1 (Boyd Exhibit 24 marked for 2 identification.) 3 QUESTIONS BY MR. RESTAINO: 4 Q. And I've marked that study as 5 Boyd 24. 6 And if you turn to this study 7 on the summary on page 2, background. 8 "Ovarian cancer has a poor prognosis, with 9 just 40 percent of patients surviving five 10 years. We designed this trial to establish 11 the effect of early detection by screening on 12 ovarian cancer mortality." 13 So a priori, they sought to 14 establish the effect of early detection by 15 screening on ovarian cancer mortality, 16 correct? 17 A. That was a horrible sentence. 18 I'm sorry. 19 Q. It wasn't -- 20 A. The purpose -- go ahead. 21 Q. It wasn't an ad hoc, after the 22 study was done. Let's take a look at it. 23 This was -- they set out to 24 look, right from the get-go, the effect of 25 early detection of screening on ovarian</p>	<p style="text-align: right;">Page 312</p> <p>1 Do you see that? 2 A. Yes. 3 Q. "The poor prognosis for ovarian 4 cancer, reference 1, motivated us to start a 5 program of screening research 30 years ago, 6 reference 2. We have since reported CA125 as 7 a predictor of ovarian cancer risk, reference 8 3 and 4, high specificity, reference 2, and 9 preliminary evidence of survival benefit, 10 reference 5, of multimodal screening using 11 CA125 interpreted with a cutoff with 12 transvaginal ultrasound as a second-line 13 test, development of a risk of ovarian cancer 14 algorithm, ROCA, for interpretation of 15 longitudinal CA125, reference 6 and 7. Use 16 of morphological criteria and second-line 17 vaginal ultrasound, reference 8, and use of 18 ROCA in a pilot, randomized controlled trial, 19 reference 9." 20 A. And you did a great job of 21 reading Dr. Ian Skates' summary of what I 22 just described to you prior to your having 23 read the summary of this clinical trial. 24 Q. Anywhere in this study do they 25 talk about the low specificity of using</p>
<p style="text-align: right;">Page 311</p> <p>1 cancer mortality? 2 A. Using a fairly complicated 3 algorithm known as ROCA -- 4 Q. Uh-huh. 5 A. -- with or without subsequent 6 TV, transvaginal, ultrasound in women based 7 on the ROCA algorithm, risk of ovarian 8 cancer, in women whose serum CA125 levels 9 rose in a consistent fashion. 10 So if you'd like me to explain 11 the clinical trial to you, I'd be happy to. 12 Q. No. 13 A. It was the largest prospective, 14 randomized clinical trial ever conducted in 15 the history of medicine, as far as I know. 16 It's very important. 17 Q. Well, let's take a look -- 18 well, if it's that important, your -- counsel 19 for Johnson & Johnson can address it with 20 you. 21 I want you to look at the 22 introduction at page 3 of 31 of the study, 23 and there they write, "The poor prognosis for 24 ovarian" -- I'm sorry, sir, it's page 3 of 25 31. Introduction.</p>	<p style="text-align: right;">Page 313</p> <p>1 CA125? 2 A. Well, it's important to take 3 the verbiage in this paper in context. Ian 4 Jacobs, God bless him, spent, as he 5 indicates, 30 years of his life attempting to 6 develop the CA125 marker in one or another 7 context, in this case the ROCA algorithm, 8 followed by TVU, as an early detection marker 9 for ovarian cancer in order to reduce 10 morbidity and mortality from ovarian cancer. 11 And over the years, over the 12 30 years -- again, I have great respect for 13 Ian, as well as Steven Skates, the last 14 author who developed the ROCA algorithm, as 15 scientists and clinicians. I actually worked 16 with Ian back in the day when he was doing 17 some research in Durham. 18 And over the years, they 19 published many studies showing relatively 20 high specificity and sensitivity and accuracy 21 and so forth, which led them to launch this 22 monumental 200,000-woman clinical trial over 23 a 14-year period, which failed to show that 24 CA125, using the ROCA algorithm in 25 combination with TVU, was an effective early</p>

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<p>1 detection marker for ovarian cancer, using</p> <p>2 survival from ovarian cancer as the primary</p> <p>3 end point.</p> <p>4 And it was sad for all of us,</p> <p>5 but that's the reality of the study and the</p> <p>6 fate of CA125 as we sit here today as an</p> <p>7 effective marker for the early detection of</p> <p>8 ovarian cancer.</p> <p>9 (Boyd Exhibit 25 marked for</p> <p>10 identification.)</p> <p>11 QUESTIONS BY MR. RESTAINO:</p> <p>12 Q. Let's take a look one more in</p> <p>13 this area before we move on. Another paper</p> <p>14 titled "Early Detection of Ovarian Cancer,"</p> <p>15 which I've marked as 25, by Elias.</p> <p>16 Have you seen this paper</p> <p>17 before, sir?</p> <p>18 A. Probably. I try to read most</p> <p>19 things Bob Bast writes.</p> <p>20 Q. And you see this was published</p> <p>21 in Hematology and Oncological Clinics of</p> <p>22 North America last year, 2018, correct?</p> <p>23 A. Yes.</p> <p>24 Q. And if you look at the key</p> <p>25 points, first key point on the first page is,</p>	<p>1 Q. They've got a section there</p> <p>2 titled "Protein Biomarkers." And there,</p> <p>3 writing in 2018, they write, "CA125 remains</p> <p>4 the most sensitive and specific protein</p> <p>5 biomarker for detecting early stage disease</p> <p>6 in apparently healthy populations."</p> <p>7 Did I read that correctly?</p> <p>8 A. You did.</p> <p>9 Q. And that's in conflict to what</p> <p>10 you write in your expert report; is that</p> <p>11 correct?</p> <p>12 A. Where are we reading from my</p> <p>13 expert report?</p> <p>14 I'll only add with respect to</p> <p>15 the sentence that you read that for the fifth</p> <p>16 or sixth time, CA125 is the only known</p> <p>17 biomarker for epithelial ovarian cancer, so,</p> <p>18 thus, it's arguably the most effective, which</p> <p>19 is not very.</p> <p>20 Q. Okay. So --</p> <p>21 A. I'm happy to answer the second</p> <p>22 part related to my expert report, if you'd</p> <p>23 like to point out the sentence that --</p> <p>24 Q. Do you disagree that CA125</p> <p>25 remains the most sensitive and specific</p>
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<p>1 "Given the low prevalence of ovarian cancer</p> <p>2 even among postmenopausal women, 1 to 2,500,</p> <p>3 an effective screening strategy requires high</p> <p>4 sensitivity, open paren, greater than</p> <p>5 75 percent, close paren, and extremely high</p> <p>6 specificity, open paren, 99.7 percent, close</p> <p>7 paren."</p> <p>8 Did I read that correctly?</p> <p>9 A. I'll assume you did.</p> <p>10 Q. And they discuss the high</p> <p>11 specificity of CA125 in the previous study,</p> <p>12 the large clinical trial we discussed,</p> <p>13 correct?</p> <p>14 A. No, they did not.</p> <p>15 Q. They didn't --</p> <p>16 A. They said, in fact, that an</p> <p>17 effective screening strategy requires high</p> <p>18 sensitivity and extremely high specificity.</p> <p>19 Q. Okay.</p> <p>20 A. They made no reference to</p> <p>21 having achieved 99.7 percent specificity in</p> <p>22 any context.</p> <p>23 Q. Let's go to page 906 of the</p> <p>24 Elias study.</p> <p>25 A. Okay.</p>	<p>1 protein biomarker for detecting early stage</p> <p>2 disease in apparently healthy populations?</p> <p>3 MS. MILLER: Objection. Asked</p> <p>4 and answered. Multiple times.</p> <p>5 THE WITNESS: Is it okay to</p> <p>6 agree with defense counsel?</p> <p>7 MS. MILLER: No.</p> <p>8 MR. RESTAINO: Yes.</p> <p>9 MS. MILLER: Then they'll</p> <p>10 accuse me of coaching. Please don't</p> <p>11 do that.</p> <p>12 THE WITNESS: Oh, I see.</p> <p>13 I'm sorry, what was the</p> <p>14 question?</p> <p>15 QUESTIONS BY MR. RESTAINO:</p> <p>16 Q. Do you agree that CA125 in 2018</p> <p>17 remains the most sensitive and specific</p> <p>18 protein biomarker for detecting early stage</p> <p>19 disease in apparently healthy populations?</p> <p>20 MS. MILLER: Objection.</p> <p>21 THE WITNESS: And for the</p> <p>22 seventh time, yes, because it's the</p> <p>23 only biomarker for ovarian cancer.</p> <p>24 Thus, by definition, it would have to</p> <p>25 be the most sensitive, specific and</p>

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<p style="text-align: right;">Page 318</p> <p>1 effective, even though it's not</p> <p>2 effective in reducing mortality from</p> <p>3 ovarian cancer, as evidenced by the</p> <p>4 largest randomized, prospective,</p> <p>5 controlled clinical trial ever</p> <p>6 conducted in the history of medicine.</p> <p>7 QUESTIONS BY MR. RESTAINO:</p> <p>8 Q. Reducing mortality is an</p> <p>9 entirely different end point than early</p> <p>10 detection; isn't it correct?</p> <p>11 A. Well, what's the point of early</p> <p>12 detection if you're not going to reduce</p> <p>13 mortality?</p> <p>14 Q. Two different studies. Would</p> <p>15 you agree a study for -- that has a primary</p> <p>16 end point of early detection is entirely</p> <p>17 different from a study whose primary end</p> <p>18 point is decreased mortality?</p> <p>19 MS. MILLER: Objection.</p> <p>20 THE WITNESS: If such</p> <p>21 hypothetical studies existed, I would</p> <p>22 agree that the end points that you</p> <p>23 are -- that you articulated are indeed</p> <p>24 different end points.</p> <p>25 I personally, given the amount</p>	<p style="text-align: right;">Page 320</p> <p>1 cell line studies alone and the increase in</p> <p>2 CA125, while intriguing, are not sufficiently</p> <p>3 convincing."</p> <p>4 Did I read that correctly?</p> <p>5 A. You did.</p> <p>6 Q. Now, do you agree that the</p> <p>7 manuscript was well-written?</p> <p>8 A. No. It was horribly written.</p> <p>9 Q. Okay.</p> <p>10 A. It was impossible to follow, in</p> <p>11 fact, in my opinion.</p> <p>12 Q. Do you agree that the</p> <p>13 conclusions were supported by the results?</p> <p>14 A. No.</p> <p>15 Q. Do you agree that this is an</p> <p>16 important but controversial topic?</p> <p>17 A. What's the topic?</p> <p>18 Q. Regarding inflammation -- talc,</p> <p>19 inflammation and ovarian cancer.</p> <p>20 A. Hard to say.</p> <p>21 Q. Regarding this --</p> <p>22 MS. MILLER: Are you done with</p> <p>23 your answer? You sounded like you</p> <p>24 were continuing.</p> <p>25 THE WITNESS: I'm done.</p>
<p style="text-align: right;">Page 319</p> <p>1 of work that's gone into the study of</p> <p>2 CA125 as a predictive marker for the</p> <p>3 early detection of ovarian cancer,</p> <p>4 would suggest that the only reason for</p> <p>5 having pursued those studies over</p> <p>6 30 years would have been to reduce</p> <p>7 mortality from ovarian cancer. And</p> <p>8 I'll stop there.</p> <p>9 QUESTIONS BY MR. RESTAINO:</p> <p>10 Q. Okay. Let's turn to page 9 of</p> <p>11 your expert report, the last paragraph, and</p> <p>12 then we'll take a break.</p> <p>13 A. Thank you.</p> <p>14 Q. You're welcome.</p> <p>15 Are you there, sir?</p> <p>16 A. Last paragraph on page 9?</p> <p>17 Q. Page 9.</p> <p>18 "These opinions are generally</p> <p>19 shared by reviewer number 1, who provided a</p> <p>20 critique of Dr. Saed's manuscript following</p> <p>21 submission to Gynecologic Oncology. The</p> <p>22 reviewer writes that, quote, the significance</p> <p>23 of the study would be greatly enhanced if a</p> <p>24 mouse model corroborated the cell line</p> <p>25 findings. In this reviewer's opinion, the</p>	<p style="text-align: right;">Page 321</p> <p>1 Please.</p> <p>2 QUESTIONS BY MR. RESTAINO:</p> <p>3 Q. Would you agree the</p> <p>4 significance of the study would be enhanced</p> <p>5 if a mouse model corroborated the cell line</p> <p>6 findings?</p> <p>7 A. With respect to what?</p> <p>8 Q. The significance of the study.</p> <p>9 A. Well --</p> <p>10 MS. MILLER: Do you want to</p> <p>11 show us where you're reading from?</p> <p>12 THE WITNESS: He's reading, I</p> <p>13 think, the reviewer comments.</p> <p>14 MS. MILLER: Do you want to go</p> <p>15 back to that exhibit?</p> <p>16 THE WITNESS: Yeah, perhaps I</p> <p>17 should.</p> <p>18 I thought we were done, I'm</p> <p>19 sorry, with that particular document.</p> <p>20 MS. MILLER: Do you remember</p> <p>21 what number it is?</p> <p>22 Do you want me to go through</p> <p>23 the file and pull it?</p> <p>24 MS. EMMEL: It is Exhibit 19, I</p> <p>25 believe.</p>

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<p style="text-align: right;">Page 322</p> <p>1 THE WITNESS: Did we go through 2 them in order? So in other words, 3 I'll find Exhibit 19 before 20? 4 MS. MILLER: Theoretically. 5 THE WITNESS: Yes, here it is. 6 QUESTIONS BY MR. RESTAINO: 7 Q. And I was reading from, whether 8 it's paragraph number 1 or bullet point 9 number 1, one of the reviewers that states 10 the significance of this study. 11 A. Yes, and I'm, for the record, 12 correlating my remarks in my expert report 13 with the location in the Gynecologic Oncology 14 review document. And I'm simply quoting the 15 reviewer to some extent, hence the quotation 16 marks. 17 Q. Okay. So I'm asking? When the 18 reviewer says, "The significance of the study 19 would be greatly enhanced if a mouse model 20 corroborated the cell line findings," do you 21 agree? 22 A. No, I believe the study has no 23 inherent significance. 24 Q. Okay. 25 A. As presented. And so</p>	<p style="text-align: right;">Page 324</p> <p>1 A. Yes. 2 Q. SNPs, for the court reporter. 3 -- "identified by the Dr. Saed 4 in his background discussion of ovarian 5 cancer-associated polymorphisms was observed 6 in his talc study." 7 Did I read that correctly? 8 A. Yes. 9 Q. Did any of the peer reviewers 10 bring out that observation? 11 A. I think there was one comment 12 by the peer reviewers on the whole genotype 13 switching mess. 14 Reviewer 1 stated in his or her 15 second comment: "The significance of SNP 16 alterations should be further clarified." 17 Q. And that is something that can 18 be done with a subsequent experiment, 19 correct? 20 A. No, I honestly think that he or 21 she was referring to the -- had the same 22 response that I did inasmuch as the data were 23 just indescribably confusing in terms of 24 hypothesis and conclusion. 25 Q. Where does any of those words</p>
<p style="text-align: right;">Page 323</p> <p>1 reproducing insignificant, tortured, 2 illogical findings in a mouse model would not 3 increase the veracity of the data presented 4 in the paper published in Reproductive 5 Biology -- I'm sorry, I can't remember the 6 journal in which it ultimately appeared. 7 MR. RESTAINO: Okay. Why don't 8 we go ahead and take a break at this 9 point. 10 VIDEOGRAPHER: Off the record 11 at 4:08 p.m. 12 (Off the record at 4:08 p.m.) 13 VIDEOGRAPHER: We're back on 14 the record at 4:21 p.m. 15 QUESTIONS BY MR. RESTAINO: 16 Q. Doctor, as we wind down to the 17 11 -- proverbial eleventh hour, will you turn 18 to page 12 of your expert report? And the 19 first full paragraph starts off with a 20 bolded, italicized "second." 21 Do you see that, sir? 22 A. I do. 23 Q. "Second, none of the SNP" -- 24 A. SNPs. 25 Q. I can say "snips"?</p>	<p style="text-align: right;">Page 325</p> <p>1 appear in the peer reviewer's notes? 2 A. They don't. I'm making -- I'm 3 making an inference. 4 Q. Okay. 5 A. By what I'm reading. 6 Q. Now -- 7 A. If I had received this review, 8 that would say to me that I need to explain 9 better what the heck it was I was trying to 10 show in my paper, not that I needed to do 11 more experiments. 12 Q. Can reasonable scientists 13 disagree with your interpretation of that 14 review and proceed differently? 15 A. Sure. It's getting late. 16 Q. In the middle of the paragraph, 17 you have -- you discuss a meta-analysis of 43 18 case-control studies. 19 Do you see that, sir? 20 A. Yes. 21 Q. A meta-analysis of 43 22 case-control studies involving various types 23 of cancer found no association between the RS 24 2333227 polymorphism, open paren, MPO, close 25 paren, and an increased cancer risk."</p>

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<p>1 Did I read that correctly?</p> <p>2 A. You did.</p> <p>3 Q. And what was the purpose of you</p> <p>4 including that meta-analysis in your report?</p> <p>5 A. You know, this is a very long</p> <p>6 and dense section written two months ago, and</p> <p>7 furthermore, the reason it's very long and</p> <p>8 dense is because I was doing my best to</p> <p>9 interpret an incredibly dense series of</p> <p>10 experiments and point out why in my mind they</p> <p>11 were flawed.</p> <p>12 So to be honest with you, I</p> <p>13 just simply can't take a sentence out of</p> <p>14 four-page commentary on the SNP experiments</p> <p>15 and do this deposition justice. I'm sorry.</p> <p>16 Q. Did you review your expert</p> <p>17 report in preparation --</p> <p>18 A. Of course I did.</p> <p>19 (Boyd Exhibit 26 marked for</p> <p>20 identification.)</p> <p>21 QUESTIONS BY MR. RESTAINO:</p> <p>22 Q. Okay. I've now marked as an</p> <p>23 exhibit the Chu, et al., meta-analysis titled</p> <p>24 "The MPO -463 G, greater than symbol, A</p> <p>25 polymorphism and cancer risk: A</p>	<p>1 there.</p> <p>2 So, first of all, it would seem</p> <p>3 that the authors of this paper on this</p> <p>4 particular polymorphic variant are opining on</p> <p>5 the free radicals exceeding antioxidant</p> <p>6 defense mechanisms, generally speaking, in</p> <p>7 cancer development, not in ovarian cancer</p> <p>8 specifically.</p> <p>9 And then the title of the paper</p> <p>10 referenced is "Oxidative stress inactivates</p> <p>11 the human DNA mismatch repair system," so I'm</p> <p>12 not really sure how DNA mismatch repair,</p> <p>13 which is one of four major mechanisms of DNA</p> <p>14 repair in mammals, is relevant to this whole</p> <p>15 sentence preceding the reference.</p> <p>16 Q. Okay. This is a peer-reviewed,</p> <p>17 published paper in Mutagenesis, correct?</p> <p>18 A. Correct, but my answer stands.</p> <p>19 Q. And this is a reference in your</p> <p>20 expert report, correct?</p> <p>21 A. The Mutagenesis paper.</p> <p>22 Q. Yes.</p> <p>23 A. Question mark.</p> <p>24 Q. Okay. Now, the right column of</p> <p>25 the first page, last full paragraph</p>
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<p>1 meta-analysis based on 43 case-control</p> <p>2 studies," Mutagenesis.</p> <p>3 Did I read that correctly?</p> <p>4 A. Yes.</p> <p>5 Q. If you look at the first page,</p> <p>6 the left column, Introduction, they start off</p> <p>7 by saying, "Cancer is a multifactorial</p> <p>8 disease that results from complex</p> <p>9 interactions between the environmental and</p> <p>10 genetic factors."</p> <p>11 Did I read that correctly?</p> <p>12 A. You did.</p> <p>13 Q. And we discussed that earlier</p> <p>14 today, correct?</p> <p>15 A. Many times.</p> <p>16 Q. Yes.</p> <p>17 And then the next sentence is</p> <p>18 that "Evidence suggests that oxidative</p> <p>19 stress, defined as a state where the levels</p> <p>20 of free radicals exceed antioxidant defense</p> <p>21 mechanism, plays a crucial role in cancer</p> <p>22 development," reference number 2.</p> <p>23 Did I read that correctly?</p> <p>24 A. Yes, you did, so let's look at</p> <p>25 reference number 2 and then take it from</p>	<p>1 between -- before materials and methods.</p> <p>2 If you see that, you look up,</p> <p>3 they start off the final sentence saying,</p> <p>4 "Considering the extensive role of NPO in the</p> <p>5 carcinogenic process, we performed a</p> <p>6 meta-analysis of all eligible case-control</p> <p>7 studies to estimate the overall cancer risk</p> <p>8 of this polymorphism and to quantify the</p> <p>9 potential between studied heterogeneity."</p> <p>10 Did I read that correctly?</p> <p>11 A. Yes, you did.</p> <p>12 Q. Would you agree that</p> <p>13 heterogeneity is an inherent limitation in</p> <p>14 meta-analyses?</p> <p>15 A. I'm sorry, I'm just trying to</p> <p>16 keep up. Could you restate the question?</p> <p>17 Q. Would you agree that the</p> <p>18 concept of heterogeneity is an inherent</p> <p>19 limitation in meta-analyses?</p> <p>20 A. I have a two-pronged answer.</p> <p>21 Actually, it's only one.</p> <p>22 My simple answer is this: I'm</p> <p>23 not an expert in epidemiologic studies, and I</p> <p>24 have no -- I can't answer the question.</p> <p>25 Q. Okay. In this study, I think</p>

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<p style="text-align: right;">Page 330</p> <p>1 you reference -- if you look at page 391, 2 there's a Table 1. And if you look at the 43 3 studies here making up this meta-analysis, 4 can you share with the Court how many studies 5 from this meta-analysis which you are relying 6 upon for your expert opinion in this matter 7 involve ovarian cancer? 8 MS. MILLER: Objection. 9 THE WITNESS: One, question 10 mark? 11 QUESTIONS BY MR. RESTAINO: 12 Q. The Olson 2004 study? 13 A. Sorry, I've got to find it 14 again. The Olson 2004 appears to say 15 "ovarian cancer," yes, with 122 cases and 396 16 controls. 17 Q. And if you just scroll through 18 the cancer type column, just roughly 19 speaking, would you agree that most of the -- 20 of the studies involved lung cancer? 21 A. That's a fair statement. 22 Q. Would you agree that there are 23 different genetic components and risk factors 24 associated with lung cancer as there is with 25 ovarian cancer?</p>	<p style="text-align: right;">Page 332</p> <p>1 Please repeat your current 2 question. 3 MS. MILLER: Wait. Wait. 4 Do you need to clean up your 5 last answer or explain -- or what are 6 you saying? 7 THE WITNESS: No. Apparently I 8 was citing this paper, Chu, et al., 9 and I'm willing to let it go at this 10 point. 11 QUESTIONS BY MR. RESTAINO: 12 Q. Okay. The question that I 13 asked now, Doctor, is, did you find any, as 14 you described them, invariably smudged 15 handwritten page numbers which contributed in 16 your opinion to the overall results of the 17 study? 18 MS. MILLER: Objection. 19 THE WITNESS: Well, again, with 20 all due respect, sir, that's a bizarre 21 question. 22 I -- looking through that 23 particular notebook, I found that 24 every single page number had either 25 been, in my opinion, whited out and</p>
<p style="text-align: right;">Page 331</p> <p>1 A. I'm sorry, could you repeat the 2 question? 3 Q. Would you agree that there are 4 different genetic components and risk factors 5 associated with lung cancer as compared to 6 ovarian cancer? 7 A. Yes. 8 Q. Do you understand the concept 9 of external validity as it relates to 10 epidemiological studies? 11 A. I'm not going to comment on 12 epidemiologic studies, and especially 13 methodology underlying epidemiologic studies. 14 That's not my area of expertise. 15 Q. Okay. Doctor, did you find any 16 invariably smudged handwritten page numbers 17 which substantively affected the results of 18 the study? 19 A. I'm sorry, I got sidetracked, 20 but we've gone past the question. 21 The polymorphism as I described 22 it in my expert report was based on its 23 description in the human genome, whereas this 24 paper was looking -- it's a retrospective 25 comment.</p>	<p style="text-align: right;">Page 333</p> <p>1 written over or erased and written 2 over, which, in my mind, generally 3 speaking, calls into question the 4 validity of every shred of data on 5 every one of those pages, and when it 6 was performed and how it was 7 performed, and so on and so forth. 8 One simply does not change 9 every page number in a laboratory 10 notebook. 11 QUESTIONS BY MR. RESTAINO: 12 Q. Your expert report on page 23, 13 the top paragraph, the very first full 14 paragraph -- and I'll wait for you to get 15 there. I'm sorry. 16 A. It's all right. 17 Q. You write, "Regardless, if one 18 considers the data table in question, the 19 first horizontal row concludes on the far 20 right with a, quote, average, end quote, 21 value of 11.07 for three replicative values 22 of 9.98, 11.63, and 10.50, reference 99. The 23 correct average would have been 10.70." 24 Did I read that correctly, sir? 25 A. Yes.</p>

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<p style="text-align: right;">Page 334</p> <p>1 Q. Is that data in the final 2 published manuscript? 3 A. No, he doesn't publish the raw 4 data in the final manuscript. 5 Q. And in any of the graphs in the 6 final manuscript, are the graphs specific 7 enough to show what that difference in 8 average would show? 9 A. That's a great question, and 10 the answer is no. It's impossible to discern 11 from the histograms in the final paper which 12 numbers the histograms actually represent. 13 Absolutely impossible. 14 One can at best come up with a 15 rough estimate based on the Y axis of what 16 the histograms represent. 17 Q. Regarding the Dr. Saed -- or 18 Fletcher, et al.'s, published paper 19 disclosure regarding the declaration of a 20 conflict of interest, it's your expert 21 opinion that the published conflict of 22 interest statement is inappropriate? Is that 23 correct? 24 A. Well, first, let's just be 25 clear. When I wrote my expert opinion, the</p>	<p style="text-align: right;">Page 336</p> <p>1 I can tell from the chain of events, the 2 version of the manuscript that was accepted 3 by the journal -- and I apologize, 4 Reproductive Sciences, but we're all familiar 5 with the name of the journal, I think -- did 6 not at that time have the declaration. 7 Q. Okay. 8 A. And so the reviewers, the two 9 or more individuals who would have judged, in 10 addition to the science, any potential 11 influence that a conflict of interest may 12 have had on the explication of the science, 13 they were unaware of that relationship, to 14 the extent that the relationship is 15 adequately defined. And that's the second 16 problem with the declaration. 17 So first, the reviewers didn't 18 see it when they accepted the paper. 19 Second, it's a completely 20 open-ended declaration of conflict. In other 21 words, if I were reviewing the paper and knew 22 that he was a paid consultant for plaintiffs 23 in the litigation, which of course his paper 24 supports, then that would very much factor 25 into my opinion as opposed to a paid</p>
<p style="text-align: right;">Page 335</p> <p>1 only manuscript I had available to review had 2 no acknowledgements or declarations of 3 conflicting interests. And so naturally I 4 would write an expert report that found that 5 to be completely unacceptable under the 6 circumstances. 7 Q. Is your opinion different today 8 based upon the published article itself? 9 A. Not in a substantial way, and 10 I'll tell you why. 11 First, while I would like to 12 think he took my critique to heart and 13 decided to include a declaration of 14 conflicting interests in the ultimate 15 published version of the paper where he says 16 some other stuff about -- in his preface, the 17 gist of the declaration is that Dr. Saed has 18 served as a paid consultant, an expert 19 witness, in the talcum powder litigation. 20 Q. Okay. 21 A. And in my mind, there are two 22 major problems with this declaration. 23 First, as memory serves -- and 24 I received multiple copies of the manuscript 25 over time from defense attorneys. As far as</p>	<p style="text-align: right;">Page 337</p> <p>1 consultant for defense representing Johnson & 2 Johnson. 3 Q. That wouldn't factor into your 4 opinion? 5 A. No, it certainly would. I'm 6 just simply stating it's a binary. 7 Q. Okay. 8 A. So in other words, you're 9 either a paid consultant, an expert witness, 10 for plaintiffs or for defense. 11 Q. Okay. Is it -- 12 A. And he doesn't specify. And so 13 it's a meaningless declaration of conflict. 14 Q. Okay. Is it your opinion that 15 a scientist is likely to bias his 16 experimental results in a way that favors 17 whoever funded him or her? 18 A. I'm not going to comment on 19 individuals and their motives. I'm going to 20 comment on how I interpret this completely 21 meaningless declaration of conflicting 22 interests. 23 Q. Okay. 24 A. It was not present when the 25 paper was accepted and is meaningless after</p>

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<p style="text-align: right;">Page 338</p> <p>1 he added it in terms of which side he was</p> <p>2 serving as an expert witness on.</p> <p>3 Q. Are you a biased witness</p> <p>4 inasmuch as you're being paid \$1,200 an hour</p> <p>5 by Johnson & Johnson?</p> <p>6 A. No.</p> <p>7 Q. Do you have any reason to</p> <p>8 believe any of the plaintiff experts are</p> <p>9 biased because they're being paid by the</p> <p>10 plaintiffs?</p> <p>11 A. Actually, it's my impression</p> <p>12 that plaintiffs, based on Dr. Saed's</p> <p>13 deposition transcript, funded -- well, it's</p> <p>14 very murky.</p> <p>15 Q. And I'm sorry, sir, I was just</p> <p>16 referring to the other plaintiff experts who</p> <p>17 have performed -- who written expert reports</p> <p>18 like yourself.</p> <p>19 Are they biased because</p> <p>20 plaintiff attorneys are paying them?</p> <p>21 MS. MILLER: He's trying to</p> <p>22 answer a question, and you interrupted</p> <p>23 him.</p> <p>24 THE WITNESS: I believe that</p> <p>25 it's quite possible that Dr. Saed was</p>	<p style="text-align: right;">Page 340</p> <p>1 cancer.</p> <p>2 I would agree with my statement</p> <p>3 if -- and if it's an accurate reflection of</p> <p>4 your question, then the answer is yes.</p> <p>5 Q. I would adopt that, sir.</p> <p>6 If prevention strategies are to</p> <p>7 be developed, would you agree that</p> <p>8 sophisticated markers for risks are needed,</p> <p>9 such as SNPs, epidemiology and lifestyle?</p> <p>10 MS. MILLER: Objection.</p> <p>11 THE WITNESS: Well, that's a</p> <p>12 very bad sentence. I'm sorry, sir.</p> <p>13 QUESTIONS BY MR. RESTAINO:</p> <p>14 Q. Oh, Okay.</p> <p>15 A. Epidemiology is not a marker,</p> <p>16 for example.</p> <p>17 Q. Okay. March 2007, did you</p> <p>18 attend a conference in Lake Como, Italy?</p> <p>19 A. I certainly attended a</p> <p>20 conference in Lake Como, Italy. It was</p> <p>21 beautiful. I can't honestly say when it was.</p> <p>22 Q. To refresh your memory, does it</p> <p>23 sound like the 11th ovarian cancer</p> <p>24 action/HHMT forum, Lake Como --</p> <p>25 A. Helene Harris Memorial Trust,</p>
<p style="text-align: right;">Page 339</p> <p>1 biased based on the fact he was being</p> <p>2 paid to write this paper.</p> <p>3 QUESTIONS BY MR. RESTAINO:</p> <p>4 Q. I'm sorry?</p> <p>5 A. With respect to other</p> <p>6 plaintiffs' expert witnesses, obviously I</p> <p>7 have no reason to think that they would have</p> <p>8 been biased.</p> <p>9 Q. Do you agree that the</p> <p>10 identification of women at an increased risk</p> <p>11 for ovarian cancer will facilitate the</p> <p>12 prevention and early detection in some</p> <p>13 patients?</p> <p>14 A. I'm sorry --</p> <p>15 MS. MILLER: Objection.</p> <p>16 THE WITNESS: Please repeat.</p> <p>17 QUESTIONS BY MR. RESTAINO:</p> <p>18 Q. Do you agree that the</p> <p>19 identification of women at increased risk for</p> <p>20 ovarian cancer will facilitate prevention and</p> <p>21 early detection in some patients?</p> <p>22 A. So if I can restate, the</p> <p>23 identification of women at increased risk for</p> <p>24 ovarian cancer could potentially result in</p> <p>25 primary or secondary prevention of said</p>	<p style="text-align: right;">Page 341</p> <p>1 yes, that rings a bell.</p> <p>2 Q. Next question.</p> <p>3 That meeting is held every four</p> <p>4 years; is that correct?</p> <p>5 A. Used to be. I think it's</p> <p>6 petered out over the years, but --</p> <p>7 unfortunately. But at that time, I think it</p> <p>8 was actually held every two years,</p> <p>9 alternating between Europe and the United</p> <p>10 States.</p> <p>11 But go ahead, please.</p> <p>12 Q. Were you a delegate at the</p> <p>13 meeting?</p> <p>14 A. At that particular meeting?</p> <p>15 Q. Yes.</p> <p>16 MS. MILLER: 12 years ago?</p> <p>17 MR. RESTAINO: Yes.</p> <p>18 THE WITNESS: In 2007?</p> <p>19 QUESTIONS BY MR. RESTAINO:</p> <p>20 Q. Yes.</p> <p>21 A. If by "delegate" you mean was I</p> <p>22 a participant, yes.</p> <p>23 Q. Okay. As you sit here today,</p> <p>24 do you recall if Dan Cramer was a delegate at</p> <p>25 the meeting?</p>

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<p style="text-align: right;">Page 342</p> <p>1 A. I can't recall, but I'm 2 guessing he probably was or you wouldn't have 3 asked the question. 4 Q. Do you know -- 5 MS. MILLER: Please don't 6 speculate, sir. 7 THE WITNESS: Okay. Thank you. 8 QUESTIONS BY MR. RESTAINO: 9 Q. Do you know if Dr. Roberta Ness 10 was a delegate at the meeting? 11 A. No. 12 Q. And do you recall if one goal 13 of the meeting was the determination of women 14 at risk for ovarian cancer? 15 A. My memory is that most of the 16 HHMT ovarian cancer symposia or scientific 17 conferences were extremely broad in scope, 18 and I don't remember ever attending one -- I 19 only attended several -- where there was 20 special attention paid to any given topic 21 related to ovarian cancer. 22 Q. So -- 23 A. Typically it was -- again, to 24 use the term I used before, it spanned the 25 waterfront, if you will.</p>	<p style="text-align: right;">Page 344</p> <p>1 Do you recall an algorithm 2 being developed at that conference in 2007 3 which used seven risk factors, including age 4 over 45, family history of ovarian cancer, 5 early onset breast cancer, Jewish ethnicity, 6 no oral contraceptive use, no live births, no 7 breastfeeding, no tubal ligation, and 8 long-term genital talc usage? 9 Do you recall that, sir? 10 MS. MILLER: Objection. 11 THE WITNESS: Well, I'm sorry 12 to have allowed you to burn through 13 some of your important time, but as I 14 said before, the only thing I remember 15 about that meeting 12 years ago was 16 the scenery. 17 QUESTIONS BY MR. RESTAINO: 18 Q. Okay. Do you recall a 19 conference report coming out of that meeting 20 12 years ago? 21 A. Not specifically. My memory of 22 the HHMT meetings is they typically led to 23 some type of meeting summary that usually got 24 published somewhere. 25 (Boyd Exhibit 27 marked for</p>
<p style="text-align: right;">Page 343</p> <p>1 Q. So do you recall if at the 2 meeting a discussion was had regarding a 3 combination of demographic, reproductive and 4 environmental risk factors might be used to 5 develop a model that would more accurately 6 predict risk? 7 MS. MILLER: Objection. 8 THE WITNESS: In all 9 seriousness, sir, the only thing I 10 remember about the meeting is the 11 scenery. 12 QUESTIONS BY MR. RESTAINO: 13 Q. Do you remember developing -- 14 any algorithm being developed at that 15 conference which looked at seven risk factors 16 for ovarian cancer -- 17 MS. MILLER: Objection. Sorry. 18 I thought you were done. 19 QUESTIONS BY MR. RESTAINO: 20 Q. -- including age over 45? 21 MS. MILLER: Objection. Asked 22 and answered. 23 QUESTIONS BY MR. RESTAINO: 24 Q. This is going to be a long 25 question. Give me a second. Okay.</p>	<p style="text-align: right;">Page 345</p> <p>1 identification.) 2 QUESTIONS BY MR. RESTAINO: 3 Q. I've marked as our last exhibit 4 a paper titled "Opportunities and challenges 5 in ovarian cancer research, a perspective 6 from the 11th Ovarian cancer action-HHMT 7 Forum, Lake Como, March 2007." 8 And if you would turn to the 9 last page. 10 A. Sorry, I'm just trying to get 11 rid of some stuff. 12 The reference page? 13 Q. The very last page is a list of 14 authors. 15 A. Yes. 16 Q. Do you see the sixth author 17 listed there? 18 A. I recognize the guy, yeah. 19 Q. Jeffrey A. Boyd, Anderson 20 Cancer Institute, Savannah, Georgia? 21 A. That's me. 22 Q. That's you? 23 A. That's me. 24 Q. Okay. Now, if we can turn to 25 the first page, sir, the right column, the</p>

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<p style="text-align: right;">Page 346</p> <p>1 second full paragraph, you and your coauthors 2 in 2007 wrote, "A combination of demographic, 3 reproductive and environmental risk factors 4 might be used to develop a model that would 5 more accurately predict risk. One 6 preliminary algorithm using seven risk 7 factors, open paren, age over 45; long-term 8 genital talc usage; family history of ovarian 9 cancer or early onset breast cancer; Jewish 10 ethnicity; no oral contraceptive, open paren, 11 OC, close paren, use; no live births; no 12 breastfeeding; no tubal ligation, close 13 paren, show that women with six to seven of 14 these events have an odds ratio of 7.59, 15 reference 3." 16 Did I read that correctly? 17 A. I'll submit that you did. 18 Q. Do you understand that OR, as 19 used in this paragraph, stands for an odds 20 ratio? 21 A. Yes. 22 Q. Is it also fair to say that 23 since 2007 you knew that an algorithm was 24 established which in 2008, as a coauthor, you 25 published that showed a woman with six to</p>	<p style="text-align: right;">Page 348</p> <p>1 existed. 2 I mean, you can pull out 3 sentences from my papers dating back 4 to perhaps 1980, when I may have 5 published my first, and suggest that I 6 remember every paragraph and every 7 paper, or perhaps, again, with due 8 respect, in a more sinister fashion, 9 suggested that I've ignored paragraphs 10 in over 200 papers, I think is just 11 simply unfair and disingenuous. 12 QUESTIONS BY MR. RESTAINO: 13 Q. Do you think it's unfair and 14 disingenuous in a litigation where you've 15 criticized plaintiff experts for the 16 biological plausibility of talc causing 17 ovarian cancer, when in 2007 you and your 18 other delegates developed an algorithm which 19 was published in 2008 showing that women with 20 six to seven of the risk factors you 21 established then had an odds ratio of 7.59 22 for developing ovarian cancer and you left 23 that out of your expert report? 24 MS. MILLER: Objection. 25 THE WITNESS: Well, first of</p>
<p style="text-align: right;">Page 347</p> <p>1 seven of the risk factors we've been 2 discussing all day, including long-term 3 genital talcum powder usage, had an odds 4 ratio of 7.59 for the development of ovarian 5 cancer? 6 MS. MILLER: Objection. 7 Misstates the paragraph that you're 8 basing it on. 9 THE WITNESS: If we could just 10 leave out the hypothesis, what's the 11 essence of your question? Without 12 rereading all of the algorithm, 13 please, sir. 14 QUESTIONS BY MR. RESTAINO: 15 Q. You have known since the 16 conference in 2007, in your publication in 17 2008, that an algorithm was developed using 18 six to seven risk factors as we've been 19 discussing all day, and showed that a woman 20 with six to seven of these events had an OR 21 of 7.59; is that correct? 22 MS. MILLER: Same objection. 23 THE WITNESS: I would suggest 24 that I haven't known since the day I 25 read this paper that these data</p>	<p style="text-align: right;">Page 349</p> <p>1 all, let's go back to your implication 2 that I was involved in the development 3 of the algorithm. I wasn't. 4 This was, as all meetings are, 5 a conglomeration of multiple content 6 experts in multiple areas. 7 My expertise is not in the 8 development of risk factor algorithms. 9 Other authors who signed this paper 10 undoubtedly developed that algorithm. 11 My role at this meeting was to 12 explain the state of the art in terms 13 of the genetic basis of ovarian 14 cancer, if I recall. 15 QUESTIONS BY MR. RESTAINO: 16 Q. You are the coauthor of a 17 paper, peer-reviewed and published in 2008, 18 or 11 years ago, which indicated that women 19 with six to seven of the risk factors we've 20 discussed all day have a 659 percent 21 increased risk of developing ovarian cancer, 22 are you not? 23 MS. MILLER: Objection. That's 24 a false statement. That's a -- 25 there's seven objectionable things,</p>

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<p style="text-align: right;">Page 350</p> <p>1 but you don't want me to say that</p> <p>2 them, so objection with a capital</p> <p>3 o-b-g-e -- whatever you said.</p> <p>4 THE WITNESS: Sir, I honestly</p> <p>5 don't know what you're trying to get</p> <p>6 me to say, but I wasn't involved in</p> <p>7 the development of this algorithm.</p> <p>8 QUESTIONS BY MR. RESTAINO:</p> <p>9 Q. You were involved --</p> <p>10 A. Other meeting attendees were.</p> <p>11 This is not my expertise any more than some</p> <p>12 of the immunologists at this meeting had</p> <p>13 nothing to do with the sections of the paper</p> <p>14 dealing with genetic risk.</p> <p>15 Q. Instead of being listed as one</p> <p>16 of the many delegates, as listed at the back</p> <p>17 of this, you are listed as one of the</p> <p>18 coauthors of this paper --</p> <p>19 MS. MILLER: Objection.</p> <p>20 QUESTIONS BY MR. RESTAINO:</p> <p>21 Q. -- correct?</p> <p>22 MS. MILLER: Objection.</p> <p>23 That's --</p> <p>24 MS. SHARKO: Where?</p> <p>25 MS. MILLER: Where?</p>	<p style="text-align: right;">Page 352</p> <p>1 document.</p> <p>2 A. Which one?</p> <p>3 Q. The one we were just</p> <p>4 discussing.</p> <p>5 A. Okay.</p> <p>6 Q. Under Key Recommendations --</p> <p>7 A. Where are you?</p> <p>8 Q. On page 656.</p> <p>9 A. Yes, sorry, 656.</p> <p>10 Q. Do you see the key</p> <p>11 recommendations?</p> <p>12 A. Yes. I'm sorry, were you</p> <p>13 waiting for me? I'm sorry.</p> <p>14 Q. How many are there?</p> <p>15 A. One, two, three, four, five,</p> <p>16 six -- 12 or 13.</p> <p>17 Q. Was there any recommendation to</p> <p>18 suggest to women not to use talc perineally?</p> <p>19 A. No.</p> <p>20 MS. MILLER: I have nothing</p> <p>21 else.</p> <p>22 REDIRECT EXAMINATION</p> <p>23 QUESTIONS BY MR. RESTAINO:</p> <p>24 Q. In that same section, was there</p> <p>25 any recommendations regarding oral</p>
<p style="text-align: right;">Page 351</p> <p>1 MS. SHARKO: Oh, here.</p> <p>2 QUESTIONS BY MR. RESTAINO:</p> <p>3 Q. We've established that that is</p> <p>4 you, correct, Doctor?</p> <p>5 A. Yes. It's my memory that in</p> <p>6 order to be listed as a coauthor, you needed</p> <p>7 to be an invited speaker, and that's the</p> <p>8 difference between the -- all the individuals</p> <p>9 listed here who attended the meeting out of</p> <p>10 some kind of scientific or medical interest</p> <p>11 versus myself, who was invited to opine on</p> <p>12 factors related to genetic risk for ovarian</p> <p>13 cancer; not to develop or to discuss a</p> <p>14 possible epidemiologic early detection</p> <p>15 algorithm.</p> <p>16 MR. RESTAINO: Okay. I have no</p> <p>17 further questions.</p> <p>18 THE WITNESS: I guess I have no</p> <p>19 further answers.</p> <p>20 CROSS-EXAMINATION</p> <p>21 QUESTIONS BY MS. MILLER:</p> <p>22 Q. Dr. Boyd, I have just have one</p> <p>23 more question for you.</p> <p>24 A. Okay.</p> <p>25 Q. I'm going back to this</p>	<p style="text-align: right;">Page 353</p> <p>1 contraceptive usage?</p> <p>2 And it's late, and I'm not</p> <p>3 going to play games with you.</p> <p>4 Just look at the fifth bullet</p> <p>5 point, sir.</p> <p>6 A. "Raise awareness of oral</p> <p>7 contraceptive use in high-risk women carries</p> <p>8 a BRCA and in women at conventional risk."</p> <p>9 Q. Okay. Did you agree with that</p> <p>10 statement at the time?</p> <p>11 A. Yes.</p> <p>12 Q. Okay. When did you first come</p> <p>13 to your opinions regarding the association of</p> <p>14 talc powder -- of talc and ovarian cancer?</p> <p>15 A. I think you asked this question</p> <p>16 at the beginning of the deposition, and I, if</p> <p>17 I recall, answered roughly over 30 years of</p> <p>18 passive absorption of the literature, to the</p> <p>19 extent I pay attention to the ovarian cancer</p> <p>20 literature -- and I do, on a daily basis --</p> <p>21 if such literature, in fact, existed 30 years</p> <p>22 ago, that's when.</p> <p>23 MR. RESTAINO: Okay. No</p> <p>24 further questions.</p> <p>25 MS. MILLER: Thanks.</p>

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<p style="text-align: right;">Page 354</p> <p>1 VIDEOGRAPHER: This concludes 2 today's deposition. The time is 3 4:58 p.m. 4 We're off the record. 5 (Deposition concluded at 4:58 p.m.) 6 ----- 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25</p>	<p style="text-align: right;">Page 356</p> <p>1 INSTRUCTIONS TO WITNESS 2 3 Please read your deposition over 4 carefully and make any necessary corrections. 5 You should state the reason in the 6 appropriate space on the errata sheet for any 7 corrections that are made. 8 After doing so, please sign the 9 errata sheet and date it. You are signing 10 same subject to the changes you have noted on 11 the errata sheet, which will be attached to 12 your deposition. 13 It is imperative that you return 14 the original errata sheet to the deposing 15 attorney within thirty (30) days of receipt 16 of the deposition transcript by you. If you 17 fail to do so, the deposition transcript may 18 be deemed to be accurate and may be used in 19 court. 20 21 22 23 24 25</p>
<p style="text-align: right;">Page 355</p> <p>1 CERTIFICATE 2 3 I, CARRIE A. CAMPBELL, Registered 4 Diplomate Reporter, Certified Realtime 5 Reporter and Certified Shorthand Reporter, do 6 hereby certify that prior to the commencement 7 of the examination, Jeffrey A. Boyd, Ph.D. 8 was duly sworn by me to testify to the truth, 9 the whole truth and nothing but the truth. 10 I DO FURTHER CERTIFY that the 11 foregoing is a verbatim transcript of the 12 testimony as taken stenographically by and 13 before me at the time, place and on the date 14 hereinbefore set forth, to the best of my 15 ability. 16 17 I DO FURTHER CERTIFY that I am 18 neither a relative nor employee nor attorney 19 nor counsel of any of the parties to this 20 action, and that I am neither a relative nor 21 employee of such attorney or counsel, and 22 that I am not financially interested in the 23 action. 24 25 CARRIE A. CAMPBELL, NCRA Registered Diplomate Reporter Certified Realtime Reporter Notary Public Dated: April 9, 2019</p>	<p style="text-align: right;">Page 357</p> <p>1 ACKNOWLEDGMENT OF DEPONENT 2 3 4 I, _____, do 5 hereby certify that I have read the foregoing 6 pages and that the same is a correct 7 transcription of the answers given by me to 8 the questions therein propounded, except for 9 the corrections or changes in form or 10 substance, if any, noted in the attached 11 Errata Sheet. 12 13 14 15 16 17 18 19 20 21 22 23 24 25</p> <p>Jeffrey A. Boyd, Ph.D. DATE _____</p> <p>Subscribed and sworn to before me this ____ day of _____, 20 ____.</p> <p>My commission expires: _____</p> <p>Notary Public</p>

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Exhibit D

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IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF NEW JERSEY

IN RE: JOHNSON & JOHNSON
TALCUM POWDER PRODUCTS
MARKETING, SALES PRACTICES,
AND PRODUCTS LIABILITY
LITIGATION

THIS DOCUMENT RELATES TO
ALL CASES

Case No. 16-2738
(FLW) (LHG)

MDL Docket No. 2738

Friday, March 29, 2019

- - - - -

The video deposition of MICHAEL BIRRER, M.D.,
Ph.D., taken pursuant to notice, was held at
the law offices of Butler Snow, LLP, One Federal
Place, Suite 1000, 1819 Fifth Avenue North,
Birmingham, Alabama, commencing at approximately
9:03 a.m., on the above date, before Lois Anne
Robinson, Registered Diplomate Reporter,
Certified Realtime Reporter, and
Notary Public for the State of Alabama.

Michael Birrer, M.D., Ph.D.

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<p>1 VIDEOGRAPHER: 2 We are now on the record. My name is 3 Devyn Mulholland. I'm a videographer for Golkow 4 Litigation Services. Today's date is March 29th, 5 2019. The time is 9:03 a.m. 6 This video deposition is being held in 7 Birmingham, Alabama, in the matter of Talcum 8 Powder Litigation, MDL Number 2738. The deponent 9 is Michael Birrer, M.D., Ph.D. 10 Counsel will be noted on the 11 stenographic record. The court reporter is Lois 12 Robinson and will now swear in the witness. 13 MICHAEL BIRRER, M.D., PH.D., 14 the witness, after having first been 15 duly sworn to tell the truth, the whole truth, 16 and nothing but the truth, was examined and 17 testified as follows: 18 EXAMINATION 19 BY MS. THOMPSON: 20 Q Dr. Birrer, I'm Margaret Thompson, and 21 I'll be taking your deposition today. 22 You've had your deposition taken 23 before; right? 24 A Correct.</p>	<p>1 It -- it eventually went to -- to court. They 2 have a panel up there of three judges, which sort 3 of prescreens it. 4 Q And you've also submitted a previous 5 report in this case; correct? 6 MS. CURRY: 7 Object to the form. 8 A Correct. 9 MS. THOMPSON: 10 Q That was in the Swan case? Does that 11 sound familiar? 12 A Yes. 13 Q Have any of your opinions -- and that 14 was in May 2017. Does that sound right? 15 A That sounds right. 16 Q Have any of your opinions in this case 17 changed since May 2017? 18 A No. 19 Q Have any of your opinions changed since 20 you were deposed in September of 2018? 21 A No. 22 Q I guess that would be a "no" if they 23 hadn't changed since 2017. 24 A It's consistent.</p>
Page 11	Page 13
<p>1 Q Including in the talcum powder 2 litigation; correct? 3 A Yes. 4 Q Have you had your deposition taken in 5 any other situation? 6 A I gave testimony in a case, but that 7 wasn't a deposition, I don't think. No. 8 Q And when was that? 9 A That was prior to the talc. It's -- 10 probably goes back, I want to say, 2015, 2012, 11 somewhere -- 12 Q And what -- sorry. 13 A Yeah. 14 Q What was the nature of that matter? 15 A I was in Massachusetts at the time. It 16 was a delayed diagnosis case. 17 Q A medical malpractice case? 18 A Medical malpractice, yes. 19 Q Were you testifying for the plaintiff 20 or for the defendant? 21 A Defendant. 22 Q Was it a physician or a doc- -- a 23 hospital? 24 A It was both. And it was in Maine.</p>	<p>1 Q And you're aware that the purpose of 2 today is for me to gain a thorough understanding 3 of what opinions you plan to give at a hearing or 4 trial? 5 A Yes. 6 Q And the basis for those opinions; 7 right? 8 A Yes. 9 Q And your report states that your 10 opinions are given to a reasonable degree of 11 scientific and medical certainty. 12 What does that mean to you? 13 A It means that, basically, more often 14 than not, they're correct. 15 Q And you are a medical doctor as well as 16 a Ph.D. researcher; correct? 17 A Correct. 18 Q Do you currently see patients? 19 A I do. 20 Q Do you currently diagnose ovarian 21 cancer in women? 22 A Yes. 23 Q How -- do you treat women with ovarian 24 cancer?</p>

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<p style="text-align: right;">Page 14</p> <p>1 A Yes.</p> <p>2 Q And would that primarily involve the</p> <p>3 medical aspects, including chemotherapy</p> <p>4 administration?</p> <p>5 A Yes.</p> <p>6 Q Do you perform any surgical procedures?</p> <p>7 A No.</p> <p>8 Q What --</p> <p>9 A I'm a medical oncologist.</p> <p>10 Q What --</p> <p>11 A I could perform it, but it wouldn't</p> <p>12 come out very well.</p> <p>13 Q I understand.</p> <p>14 What percentage of your time involves</p> <p>15 patient care versus research?</p> <p>16 A So --</p> <p>17 MS. CURRY:</p> <p>18 Object to the form.</p> <p>19 A -- right now I have a half-a-day clinic</p> <p>20 a week, and then the research component, I have a</p> <p>21 fully funded lab, probably two days a week. I'm</p> <p>22 the director of the cancer center, which also</p> <p>23 takes a fair amount of administrative</p> <p>24 responsibility.</p>	<p style="text-align: right;">Page 16</p> <p>1 A Yes.</p> <p>2 Q And does that pretty much cover the</p> <p>3 types of research that you would be doing in your</p> <p>4 lab --</p> <p>5 MS. CURRY:</p> <p>6 Object to the form.</p> <p>7 MS. THOMPSON:</p> <p>8 Q -- or in a general sense?</p> <p>9 A I'm just trying to think if there was</p> <p>10 anything else. We obviously do a lot of</p> <p>11 review-type papers and articles. You know, I</p> <p>12 think that's pretty broad. I think it does,</p> <p>13 actually.</p> <p>14 Q When you do a review article, is that</p> <p>15 usually invited by the journal, or is that a</p> <p>16 topic that you have interest in that you submit</p> <p>17 as a publication?</p> <p>18 A Could be both. A lot of them are</p> <p>19 invited. But we have occasionally thought of</p> <p>20 areas that we thought were interesting and</p> <p>21 important and suggested it.</p> <p>22 Q And are authors or review articles</p> <p>23 generally intended to be experts in the field?</p> <p>24 MS. CURRY:</p>
<p style="text-align: right;">Page 15</p> <p>1 MS. THOMPSON:</p> <p>2 Q So administrative time --</p> <p>3 A Yeah.</p> <p>4 Q -- as well included in that?</p> <p>5 And how would you describe the focus of</p> <p>6 your laboratory search -- research currently?</p> <p>7 A Almost entirely on ovarian cancer and</p> <p>8 exploring detailing the genomics, the molecular</p> <p>9 basis for ovarian cancer and trying to translate</p> <p>10 that into better early detection, diagnosis and</p> <p>11 treatment.</p> <p>12 Q Are you doing in vitro as well as in</p> <p>13 vivo research?</p> <p>14 A Correct.</p> <p>15 Q And have published in both animal</p> <p>16 studies as well as cellular studies?</p> <p>17 A Yes.</p> <p>18 Q Have you published with immortalized</p> <p>19 cells?</p> <p>20 A Yes.</p> <p>21 Q Have you published research with human</p> <p>22 tissue?</p> <p>23 A Yes.</p> <p>24 Q Have you published human trials?</p>	<p style="text-align: right;">Page 17</p> <p>1 Object to the form.</p> <p>2 A More often than not, yes. But</p> <p>3 frequently on my reviews, I'll have some junior</p> <p>4 people.</p> <p>5 MS. THOMPSON:</p> <p>6 Q With -- with a senior author</p> <p>7 usually --</p> <p>8 A (Nods affirmatively.)</p> <p>9 Q -- correct?</p> <p>10 A Correct.</p> <p>11 Q And that would be, I would think,</p> <p>12 because readers of a journal want to know that</p> <p>13 it's an expert in the field that's providing the</p> <p>14 information in a review article; right?</p> <p>15 MS. CURRY:</p> <p>16 Object to the form.</p> <p>17 A I think so, yeah.</p> <p>18 MS. THOMPSON:</p> <p>19 Q Would you agree with me that it would</p> <p>20 be unethical at this point in time to design a</p> <p>21 prospective study in which women were exposed to</p> <p>22 talcum powder in the genital area and follow over</p> <p>23 time?</p> <p>24 MS. CURRY:</p>

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<p>1 Object to the form.</p> <p>2 A Prospectively and randomized and --</p> <p>3 could you just --</p> <p>4 MS. THOMPSON:</p> <p>5 Q Let's start with just prospectively.</p> <p>6 A I -- I think it would be a --</p> <p>7 interesting question. I don't think it would be</p> <p>8 valuable.</p> <p>9 Q How about a randomized trial? Would it</p> <p>10 be ethical?</p> <p>11 A No. I don't think it would be valuable</p> <p>12 at all.</p> <p>13 Q But I didn't ask about valuable.</p> <p>14 What about ethical?</p> <p>15 A Well, val- -- if it's not valuable, it</p> <p>16 should -- it wouldn't be of great concern to do</p> <p>17 that. I'm not sure what you're asking.</p> <p>18 Q Well, I'm asking if you -- if you have</p> <p>19 a carcinogen, even a possible carcinogen, you</p> <p>20 could not design and get a trial through IRB</p> <p>21 using that product and a control group; correct?</p> <p>22 MR. MIZGALA:</p> <p>23 Object to form.</p> <p>24 A I guess -- I -- I see what -- now I see</p>	<p>1 A And this is -- this is a -- let me get</p> <p>2 my glasses -- supplemental materials received by</p> <p>3 me after this was done.</p> <p>4 Q Okay.</p> <p>5 A Okay?</p> <p>6 Q And, so, "received by" you meant the</p> <p>7 lawyers for Johnson & Johnson provided those</p> <p>8 supplemental materials to you?</p> <p>9 A It was a little bit of both. I mean,</p> <p>10 some of this I wasn't privy to, so I got it</p> <p>11 provided to me, and some of these were additional</p> <p>12 articles that I was -- I pulled out.</p> <p>13 Q Okay. And I've marked as Exhibit 1</p> <p>14 your expert report.</p> <p>15 (DEPOSITION EXHIBIT NUMBER 1</p> <p>16 WAS MARKED FOR IDENTIFICATION.)</p> <p>17 MS. THOMPSON:</p> <p>18 Q Do you --</p> <p>19 Do you have a copy? You're good on</p> <p>20 that?</p> <p>21 A And mine's -- mine's thicker than</p> <p>22 yours, so -- it's got my CV in there.</p> <p>23 Q I separated out your CV. So -- well,</p> <p>24 good. But that's a good observation.</p>
Page 19	Page 21
<p>1 what you're asking.</p> <p>2 So my position on that is that talc</p> <p>3 is -- I don't believe talc is a carcinogen.</p> <p>4 MS. THOMPSON:</p> <p>5 Q I understand. But there are others</p> <p>6 that do.</p> <p>7 And, so, is it your opinion that an IRB</p> <p>8 would let a study through using what has been</p> <p>9 designated as a possible carcinogen, say, for</p> <p>10 example, IARC?</p> <p>11 MS. CURRY:</p> <p>12 Object to the form.</p> <p>13 A I have no idea.</p> <p>14 MS. THOMPSON:</p> <p>15 Q All right. So the ground rules are</p> <p>16 we'll try not to interrupt each other. Let me</p> <p>17 know if I ask a bad question or one that you</p> <p>18 don't understand, and I'll expect you to answer</p> <p>19 honestly. Fair enough?</p> <p>20 A Yes.</p> <p>21 Q If you need a break, let me know.</p> <p>22 What did you bring with you today?</p> <p>23 A I have my expert report right here.</p> <p>24 Q And is that all you brought with you?</p>	<p>1 And -- and I marked as Exhibit 2 your</p> <p>2 CV.</p> <p>3 A Okay.</p> <p>4 (DEPOSITION EXHIBIT NUMBER 2</p> <p>5 WAS MARKED FOR IDENTIFICATION.)</p> <p>6 MS. THOMPSON:</p> <p>7 Q And that should --</p> <p>8 And you're good on that, too?</p> <p>9 MS. CURRY:</p> <p>10 Thank you.</p> <p>11 MS. THOMPSON:</p> <p>12 Q That should -- those combined should be</p> <p>13 the same thickness of what you've brought.</p> <p>14 And I also brought the Notice of</p> <p>15 Deposition, which I'm going to hand you.</p> <p>16 (DEPOSITION EXHIBIT NUMBER 3</p> <p>17 WAS MARKED FOR IDENTIFICATION.)</p> <p>18 MS. THOMPSON:</p> <p>19 Q And this is the one with objections.</p> <p>20 Have you seen this before, Dr. Birrer?</p> <p>21 A Yes.</p> <p>22 Q And did you look at the request on</p> <p>23 the -- on this document?</p> <p>24 A Yes.</p>

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<p style="text-align: right;">Page 22</p> <p>1 Q Is there -- and there's nothing that 2 was responsive to any of these requests? 3 MS. CURRY: 4 Objection. Subject to the objections 5 that were made by counsel. 6 MS. THOMPSON: 7 Q Subject -- 8 MS. THOMPSON: 9 Sorry. 10 Q Subject to the objections. 11 A Yeah. 12 Q So where would you keep your file for 13 the litigation? 14 MS. CURRY: 15 And I'm sorry. Just to clarify for the 16 record, there is a small production at the back 17 that incorporates the -- 18 MS. THOMPSON: 19 Yes. 20 MS. CURRY: 21 -- invoice as well as the supplemental 22 fee schedule and the supplemental list of 23 materials. 24 MS. THOMPSON:</p>	<p style="text-align: right;">Page 24</p> <p>1 Q -- this litigation? 2 And be careful not to interrupt just 3 because it makes our court reporter's job a 4 little more difficult. 5 How much money have you been paid total 6 by Johnson & Johnson in talcum powder litigation? 7 A To date, nothing. 8 Q You haven't been paid for any of the 9 other cases that you've testified in? 10 A Correct. 11 Q Why is that? 12 A I'm a lousy businessman. I haven't 13 invoiced for Swan yet and I haven't invoiced for 14 Brower. But I can -- I can estimate the hours. 15 Q Go ahead and estimate. 16 A Swan I think is around 80 hours -- 17 Q Okay. 18 A -- because it was the initial case. It 19 was a bundled -- bundled five cases, so involved 20 a lot of review. And the deposition alone was 21 quite long. I remember like it was yesterday. 22 And, then, Brower was probably about 40 23 hours. 24 Q Okay.</p>
<p style="text-align: right;">Page 23</p> <p>1 Right. 2 Q So the supplemental material list that 3 you brought with you today, Dr. Birrer, is 4 attached to the back of this notice with 5 objections; correct? 6 A That's the same as this. Yes. 7 Q Yes. 8 A Yeah. Uh-huh. 9 Q And also attached to this -- this 10 notice with objections are your fees; correct? 11 A Correct. 12 Q And are -- are those all the invoices 13 that you have submitted thus far? 14 A Yes. 15 Q And how much -- and from -- this 16 invoice that's attached to Exhibit 3 goes through 17 March 17th. 18 How much time would you say you have 19 spent since March 17th preparing for the case? 20 A I'd say probably put another 15 hours, 21 And I haven't invoiced that yet. 22 Q Okay. And you have testified in other 23 cases for the defendants in -- 24 A Correct.</p>	<p style="text-align: right;">Page 25</p> <p>1 A And those invoices are being 2 constructed. 3 Q And you're charging those at the same 4 rate as in your fee schedule -- 5 A That's right. 6 Q -- attached to this document? 7 A That's right. 8 Q Okay. When were you first approached 9 by Johnson & Johnson as -- about serving as an 10 expert in talcum powder litigation? 11 A So that was before the -- that was the 12 Blaes or Swan case. I believe it was in 13 December, around November, December of 2016. 14 Q '16? 15 A Thank you. Time flies. 16 Q Only because I know that the report was 17 submitted in May, so -- 18 A (Nods affirmatively.) 19 Q -- I'm assuming that you didn't work 18 20 months on that -- 21 A No. 22 Q -- case. 23 And you were asked in -- for this 24 report that you just submitted, to address the</p>

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<p style="text-align: right;">Page 26</p> <p>1 biological plausibility of the plaintiffs' theory 2 that cosmetic talcum powder can cause ovarian 3 cancer. Right? 4 A Correct. 5 Q And that would be the stand- -- from 6 the standpoint of the genomics and molecular 7 biology that is your expertise; correct? 8 MS. CURRY: 9 Object to the form. 10 A So I think they were asking me in the 11 big picture the biologic plausibility of talc 12 being involved in the -- causing ovarian cancer 13 and then my scientific experience, even clinical 14 experience, would factor into -- to -- to that 15 expert opinion. 16 MS. THOMPSON: 17 Q Was that a different opinion than what 18 you were asked to provide in the previous cases 19 that you testified in? 20 MS. CURRY: 21 Object to the form. 22 A Previously -- the answer, I believe, is 23 no. But I was asked for general causation 24 before. This was a more -- somewhat more narrow</p>	<p style="text-align: right;">Page 28</p> <p>1 with an increased risk of epithelial ovarian 2 cancer? 3 A Correct. 4 Q Is it your opinion that the genital use 5 of talcum powder is not a risk factor for 6 epithelial ovarian cancer? 7 A Correct. 8 Q Is it your opinion that genital use of 9 talcum powder products does not cause ovarian 10 cancer? 11 A Correct. 12 Q Is it your opinion that the genital use 13 of talcum powder products does not cause ovarian 14 cancer in some women? 15 MS. CURRY: 16 Object to the form. 17 A Correct. 18 MS. THOMPSON: 19 Q And that would be ever. 20 MS. CURRY: 21 Object -- object to the form. 22 A No data to support that. 23 MS. THOMPSON: 24 Q Is it your opinion that the genital use</p>
<p style="text-align: right;">Page 27</p> <p>1 expert opinion. 2 MS. THOMPSON: 3 Q So in this case, you're not providing 4 general causation opinions. You're providing the 5 biological mechanism, plausibility opinions; 6 correct? 7 A Well, the title -- 8 MS. CURRY: 9 Object to the form. 10 A The title on the expert report is for 11 General Causation For the Daubert Hearing. But 12 my understanding was -- was to focus extensively, 13 if you will, on the biologic plausibility. 14 MS. THOMPSON: 15 Q And because biological plausibility is 16 part of general causation; correct? 17 A Correct. 18 Q But it's not the whole of general 19 causation. Is that your understanding? 20 A Correct. 21 Q So I want to make sure that I 22 understand your opinions. 23 Is it your opinion that the perineal 24 use of talcum powder products is not associated</p>	<p style="text-align: right;">Page 29</p> <p>1 of talcum powder does not contribute to the 2 development of epithelial ovarian cancer? 3 A Yes. 4 Q And do you say that there's no data to 5 support that as well? 6 A Correct. 7 Q Is it your opinion that genital use of 8 talcum powder does not contribute to the 9 development of ovarian cancer in some women? 10 MS. CURRY: 11 Object to the form. 12 A There's no data to support that either. 13 MS. THOMPSON: 14 Q So the answer is yes? 15 A Yes. 16 Q Is it your opinion that any proposed 17 biologic mechanism for how the genital use of 18 talcum powder products could cause epithelial 19 ovarian cancer is not plausible? 20 MS. CURRY: 21 Object to the form. 22 A I would agree with that statement. 23 It's not biologically plausible. 24 MS. THOMPSON:</p>

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<p style="text-align: right;">Page 30</p> <p>1 Q Is it your opinion that any proposed</p> <p>2 biologic mechanism for how the genital use of</p> <p>3 talcum powder products might contribute to the</p> <p>4 development of ovarian cancer is not plausible?</p> <p>5 MS. CURRY:</p> <p>6 Object to the form.</p> <p>7 A There's no data for that either.</p> <p>8 MS. THOMPSON:</p> <p>9 Q So the answer would be yes?</p> <p>10 A Yes.</p> <p>11 Q Do you intend to give opinions on</p> <p>12 whether talc particles can reach the ovaries?</p> <p>13 A I believe on my expert report and in --</p> <p>14 and I'm more than happy to talk about it --</p> <p>15 reviews the migration theories.</p> <p>16 Q Do you consider yourself to be an</p> <p>17 expert in that area?</p> <p>18 A I think that those studies are</p> <p>19 relatively straightforward and, based upon my</p> <p>20 experience that, I would be relatively easy to</p> <p>21 interpret those.</p> <p>22 Q Do you feel like you would be in a</p> <p>23 better position than a gynecologist or</p> <p>24 gynecologic oncologist?</p>	<p style="text-align: right;">Page 32</p> <p>1 Object to the form.</p> <p>2 A Correct.</p> <p>3 MS. THOMPSON:</p> <p>4 Q Are all the opinions contained in your</p> <p>5 report that you will be providing in this case?</p> <p>6 A That's a tough question to ask because</p> <p>7 I don't know what you're gonna ask me.</p> <p>8 Q Fair enough.</p> <p>9 Can you think of any areas, sitting</p> <p>10 here today, that you intend to testify in other</p> <p>11 than the migration and transport of particles and</p> <p>12 the molecular and genomics of cellular tissue</p> <p>13 response to talc?</p> <p>14 MS. CURRY:</p> <p>15 Object to the form.</p> <p>16 A Well, that's the bulk of my expert</p> <p>17 report. I'm -- again, it depends on what you ask</p> <p>18 me within the construct of general causation.</p> <p>19 I'm willing to talk about some of that.</p> <p>20 MS. THOMPSON:</p> <p>21 Q Okay. I understand.</p> <p>22 A Uh-huh.</p> <p>23 Q And you are not an epidemiologist;</p> <p>24 correct?</p>
<p style="text-align: right;">Page 31</p> <p>1 A Yes.</p> <p>2 Q Have you found any new expertise in the</p> <p>3 migration or transport of particles in the female</p> <p>4 reproductive system since 2017?</p> <p>5 MS. CURRY:</p> <p>6 Object to the form.</p> <p>7 A I'm not sure what you mean by "found</p> <p>8 any new expertise." In the literature or my own</p> <p>9 experience?</p> <p>10 MS. THOMPSON:</p> <p>11 Q Do you believe that you have more</p> <p>12 expertise in that subject than you did in 2017?</p> <p>13 A I think that it's comparable.</p> <p>14 Q So that would be no additional</p> <p>15 expertise since 2017, when you testified</p> <p>16 previously?</p> <p>17 MS. CURRY:</p> <p>18 Object to the form.</p> <p>19 A Not that I can identify as -- as we're</p> <p>20 discussing this.</p> <p>21 MS. THOMPSON:</p> <p>22 Q And same for 2018, when you gave a</p> <p>23 deposition in -- in a talcum powder case?</p> <p>24 MS. CURRY:</p>	<p style="text-align: right;">Page 33</p> <p>1 A I don't have a degree in epidemiology.</p> <p>2 But I have training.</p> <p>3 Q So would you agree that your</p> <p>4 understanding of epidemiology is general in</p> <p>5 nature?</p> <p>6 MS. CURRY:</p> <p>7 Object to the form.</p> <p>8 A So in order to be a, you know,</p> <p>9 laboratory-based scientist in this field and a</p> <p>10 clinician to treat patients, you certainly need</p> <p>11 to have an understanding of epidemiologic</p> <p>12 studies, so I have that understanding. And I</p> <p>13 think that it gives me the ability to assess</p> <p>14 epidemiologic studies and to draw conclusions</p> <p>15 from them.</p> <p>16 MS. THOMPSON:</p> <p>17 Q But if you're looking for more nuanced</p> <p>18 or more comprehensive epidemiological experience,</p> <p>19 you would look to an actual epidemiologist;</p> <p>20 correct?</p> <p>21 MS. CURRY:</p> <p>22 Object to the form.</p> <p>23 A Well, I think it would depend on the</p> <p>24 question that's being asked.</p>

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<p style="text-align: right;">Page 34</p> <p>1 MS. THOMPSON: 2 Q Well, for example, in the consortium 3 that you publish with, there are specific 4 epidemiologists that publish with the group; 5 correct? 6 A Which consortium are you referring to? 7 Q There are several? 8 A Yes. 9 Q Take -- take the Ovarian Cancer 10 Association Consortium. 11 A The GOS? 12 Q No. OCAC or -- 13 A Okay. 14 Q There are specific epidemiologists that 15 I assume are recruited to -- to provide the 16 epidemiology experience in that consortium; 17 correct? 18 A There are epidemiologists in that 19 consortium. I will point out there are lots of 20 other people and scientists. 21 Q And -- and -- and you would be sought 22 out for that type of consortium because of your 23 molecular experience; correct? 24 MS. CURRY:</p>	<p style="text-align: right;">Page 36</p> <p>1 comments, and they're all listed in terms of 2 biologic plausibility. And then, of course, I 3 spent a lot of time on Dr. Saed. 4 MS. THOMPSON: 5 Q My question, though, is which of the 6 plaintiff experts were you asked to offer 7 criticism of? 8 MS. CURRY: 9 Object to the form. 10 A So I reviewed the entire list, and 11 that's listed in the materials. I think it's on 12 page -- 13 MS. THOMPSON: 14 Q 28? 15 A -- 28 and 29. 16 Q Okay. Let's go ahead and go -- do -- 17 did you read all of these experts -- expert 18 reports? 19 A I looked through them, yes. 20 Q And each one? 21 A Correct. 22 Q All right. Let's go through each one 23 and have you tell me what you gleaned from each 24 expert report.</p>
<p style="text-align: right;">Page 35</p> <p>1 Object to the form. 2 A Well, I would add to that that I think 3 from a -- sort of a clinical standpoint we 4 provide some reality testing in terms of 5 whether -- what they're observing is actually 6 meaningful. 7 MS. THOMPSON: 8 Q Yes. So it would be for your 9 experience as a clinician in genomics and 10 molecular researcher; right? 11 A Yes. 12 Q That makes sense. 13 You're not a gynecologist or 14 gynecologic oncologist; correct? 15 A Correct. 16 Q Were you asked to offer criticism of 17 plaintiff experts and their opinions? 18 MS. CURRY: 19 Object to the form. 20 A So in my expert report, I really 21 reviewed the primary literature, and with -- with 22 then integrating that into the arguments made by 23 plaintiffs' expert witnesses. So you see in a 24 section there I began to look at individuals'</p>	<p style="text-align: right;">Page 37</p> <p>1 MS. CURRY: 2 Object to the form. 3 MS. THOMPSON: 4 Q Ann McTiernan, do you know Ann 5 McTiernan? 6 A I don't know her personally. 7 Q What's her field of expertise? 8 A I would have to check that. 9 Q So you don't remember here today 10 what -- 11 A Well, you're reviewing, I think -- 12 let's be honest, 300 pages. I'm not going to be 13 able to go through those systematically. 14 Q Well -- 15 A But if you look at my report, it very 16 specifically addressed some of the flaws in the 17 experts' opinions regarding migration of talc. 18 Q I -- I understand. But my question is 19 do you know what Dr. McTiernan's area of 20 expertise is? And it's fine if you don't. 21 A I'd have to look it up. 22 Q Okay. Do you know Dr. Carson's area of 23 expertise? 24 A I have never met him, and I don't know</p>

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<p style="text-align: right;">Page 38</p> <p>1 him.</p> <p>2 Q Have you met Dr. McTiernan?</p> <p>3 A No.</p> <p>4 Q What is Dr. Clarke-Pearson's area of</p> <p>5 expertise?</p> <p>6 A Clarke-Pearson is a gynecological</p> <p>7 oncologist, former department chair at UNC. Now</p> <p>8 he's stepped down.</p> <p>9 Q And do you know Dr. Clarke-Pearson?</p> <p>10 A I've met him.</p> <p>11 Q And what about Dr. Kessler?</p> <p>12 A I've never met Dr. Kessler.</p> <p>13 Q What's his area of expertise?</p> <p>14 A I can't quote you that.</p> <p>15 Q What's Dr. Smith's area of expertise?</p> <p>16 A I think Dr. Smith's pretty -- actually,</p> <p>17 I can't tell you.</p> <p>18 Q And Dr. Saed, I think we know.</p> <p>19 What about Dr. Siemiatycki?</p> <p>20 A Uh-uh. No.</p> <p>21 Q Dr. Wolf?</p> <p>22 A I've met Judith. She's a gynecologic</p> <p>23 oncologist.</p> <p>24 Q And do you know Dr. Zelikoff's area of</p>	<p style="text-align: right;">Page 40</p> <p>1 experiments?</p> <p>2 A No. Laboratory-based?</p> <p>3 Q Laboratory, yes.</p> <p>4 A No.</p> <p>5 Q What did you know about talcum powder</p> <p>6 and a possible link to ovarian cancer before you</p> <p>7 were approached to serve as an expert in 2017?</p> <p>8 A So it was not something that we dealt</p> <p>9 with clinically. We never counseled patients.</p> <p>10 Scientifically, it never really was part of my</p> <p>11 laboratory effort. I didn't know really -- I</p> <p>12 didn't know anybody working with it in the lab.</p> <p>13 And -- and, you know, to be fair, I would say</p> <p>14 that I was aware of the sort of concept that some</p> <p>15 people -- some epidemiologic studies were being</p> <p>16 done trying to determine relationship of talc</p> <p>17 exposure to ovarian cancer. And that's about it.</p> <p>18 Q Were you -- were you aware of the</p> <p>19 issues raised by Dr. Woodruff and others in the</p> <p>20 '70s about possible contamination with asbestos?</p> <p>21 MS. CURRY:</p> <p>22 Object to the form.</p> <p>23 A No.</p> <p>24 MS. THOMPSON:</p>
<p style="text-align: right;">Page 39</p> <p>1 expertise?</p> <p>2 A I don't know her.</p> <p>3 Q Nor her area of expertise?</p> <p>4 A Correct.</p> <p>5 Q What about Dr. Plunkett? Do you know</p> <p>6 her area of expertise?</p> <p>7 A I don't.</p> <p>8 Q Dr. Moorman, do you know her area of</p> <p>9 expertise?</p> <p>10 A Don't know her. No.</p> <p>11 Q Dr. Smith-Bindman, do you know her area</p> <p>12 of expertise?</p> <p>13 A No.</p> <p>14 Q Do you know the area of expertise of</p> <p>15 Dr. Kane?</p> <p>16 A Nope.</p> <p>17 Q Dr. Levy?</p> <p>18 A No.</p> <p>19 Q Dr. Singh?</p> <p>20 A No.</p> <p>21 Q Were you asked by Johnson & Johnson to</p> <p>22 perform any experiments?</p> <p>23 A No.</p> <p>24 Q Did you offer to perform any</p>	<p style="text-align: right;">Page 41</p> <p>1 Q Did you have any opinions about whether</p> <p>2 talcum powder could cause ovarian cancer before</p> <p>3 you were approached to serve as an expert?</p> <p>4 A Well, my sense was that it wasn't a</p> <p>5 factor.</p> <p>6 Q And what was --</p> <p>7 A Because we -- again, we weren't -- we</p> <p>8 weren't using it in the clinic. We weren't</p> <p>9 talking about it. There were essentially no</p> <p>10 presentations in the biologic plausibility within</p> <p>11 any of the scientific meetings that I would go</p> <p>12 to.</p> <p>13 Q And at that time, that's what your</p> <p>14 impression, at least, would have been based on?</p> <p>15 MS. CURRY:</p> <p>16 Object to the form.</p> <p>17 A Yeah.</p> <p>18 MS. THOMPSON:</p> <p>19 Q Did you write your report?</p> <p>20 A Yes.</p> <p>21 Q Every word?</p> <p>22 A Yes.</p> <p>23 Q Did you choose the literature to cite?</p> <p>24 A So I pulled out most of that myself,</p>

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<p style="text-align: right;">Page 42</p> <p>1 went back and did a reference list and then 2 pulled more. As I said before, the expert 3 reports would have been provided from counsel. 4 There may have been some papers that I 5 said, hey, I don't have this. Can you pull this 6 out? And then they would -- they would provide 7 it to me. 8 Q And there are -- just so I understand 9 the literature -- 10 A Uh-huh. 11 Q -- there's literature that you actually 12 cite in the report in footnotes; right? 13 A Correct. 14 Q And then there's another list at the 15 end of the report that's considered -- that's 16 titled "Materials Reviewed and Considered by Dr. 17 Birrer"; right? 18 A That's right. 19 Q And can I assume that the literature 20 that are actually cited in the footnotes is 21 literature that you felt was particularly 22 significant? 23 MS. CURRY: 24 Object to the form.</p>	<p style="text-align: right;">Page 44</p> <p>1 of information, I did that by searching. 2 MS. THOMPSON: 3 Q And what search engines did you use? 4 A It was mostly PubMed, which is 5 something we use all the time. 6 Q And did you -- what search terms did 7 you use? 8 A Ovary, ovarian cancer, talc. So the 9 ones you -- you'd predict. And that doesn't 10 necessarily generate the entire list. Right? I 11 mean, you get the list and then you look at the 12 papers, go back to the references in those 13 papers, and then you see if you -- you're missing 14 out. Then you pull out more. And as you go 15 through this iteration, you begin to find out 16 that you're identifying the same patient -- the 17 same papers. So then you begin to get an idea 18 that you have the sum total of what you need. 19 Q And have you saved those papers 20 anywhere? 21 A So those were -- the way that worked 22 was they came in, mostly computer-based, and then 23 I would look at those, extract what I wanted, and 24 then construct the report. And that was all done</p>
<p style="text-align: right;">Page 43</p> <p>1 A Yeah. So the idea here was to try to 2 provide some guidance as to where that reference 3 was relevant within the document. That's why 4 it's on each page. At the end is a sort of sum 5 total. 6 MS. THOMPSON: 7 Q Okay. 8 A Yeah. 9 Q Did you choose any quotes that are 10 included in your expert report yourself? 11 MS. CURRY: 12 Object to the form. 13 MS. THOMPSON: 14 Q It was a bad question. 15 Did you choose the quotes that are 16 included in your expert report? 17 A Correct. 18 Q Did you choose the language that you 19 used to criticize the plaintiffs' experts? 20 A Correct. 21 Q Did you perform any searches? 22 MS. CURRY: 23 Object to the form. 24 A In order to generate the original body</p>	<p style="text-align: right;">Page 45</p> <p>1 in the computer. 2 Q But what happened to the articles? 3 MS. CURRY: 4 Object to the form. 5 A Well, they'd be computer-based, or 6 there's backup, I believe, some backup copies 7 here on everything. 8 MS. THOMPSON: 9 Q So -- so everything that you looked at 10 would be in your materials considered list and 11 the supplemental materials considered list? 12 A Correct. Yep. 13 Q Did you look at plaintiff expert 14 depositions? 15 A Correct. 16 Q Which ones? 17 A So I looked at the deposition of 18 Dr. Saenz. I think that's listed on supplemental 19 deposition. 20 MS. CURRY: 21 I believe she asked about plaintiff 22 expert deposition. 23 MS. THOMPSON: 24 Q Plaintiff.</p>

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<p style="text-align: right;">Page 46</p> <p>1 A I'm sorry. I'm on the wrong one. So</p> <p>2 that would be Dr. Saed.</p> <p>3 Q Uh-huh.</p> <p>4 A And I think -- let's go back and look.</p> <p>5 I think -- yeah. It was 23 and 24 are -- were</p> <p>6 both the Saed depositions. I think that's it.</p> <p>7 Q In the file -- the backup file that you</p> <p>8 mentioned that's here, is that on a thumb drive</p> <p>9 or what's --</p> <p>10 MS. CURRY:</p> <p>11 Object to the form. They're actually</p> <p>12 my -- the lawyer's files. I just brought a copy</p> <p>13 of the references in case we needed to refer to</p> <p>14 everything. But it's not -- actually not</p> <p>15 Dr. Birrer's file.</p> <p>16 MS. THOMPSON:</p> <p>17 Q So there's no electronic file that you</p> <p>18 possess?</p> <p>19 A Yeah.</p> <p>20 Q Did you make any notes or highlights on</p> <p>21 any of the articles that --</p> <p>22 A (Shakes head negatively.)</p> <p>23 Q And in addition to Dr. Saed's</p> <p>24 deposition, you have listed two drafts of his</p>	<p style="text-align: right;">Page 48</p> <p>1 MS. CURRY:</p> <p>2 Here you go.</p> <p>3 A This supplemental list with objections</p> <p>4 or the extra paper?</p> <p>5 MS. THOMPSON:</p> <p>6 Q And you reviewed some reports from</p> <p>7 governmental and regulatory agencies; correct?</p> <p>8 A Correct.</p> <p>9 Q I'll go ahead and mark those. We're</p> <p>10 gonna discuss them more later.</p> <p>11 (DEPOSITION EXHIBIT NUMBER 4</p> <p>12 WAS MARKED FOR IDENTIFICATION.)</p> <p>13 MS. THOMPSON:</p> <p>14 Q You've looked at the Health Canada's</p> <p>15 recent draft assessment; correct?</p> <p>16 A Yes.</p> <p>17 Q When did you first see that?</p> <p>18 A It was in a deposition of Dr. Saenz's.</p> <p>19 Q And do you know when that was first</p> <p>20 published?</p> <p>21 A The Health Canada?</p> <p>22 Q Yes.</p> <p>23 A Fairly recently. Can't quote you the</p> <p>24 date.</p>
<p style="text-align: right;">Page 47</p> <p>1 manuscript that was recently published; correct?</p> <p>2 A I believe I saw the pre-print and then</p> <p>3 the copy of the actual published paper. And, of</p> <p>4 course, his expert report.</p> <p>5 Q When did you first see Dr. Saed's</p> <p>6 manuscript?</p> <p>7 MS. CURRY:</p> <p>8 Object to the form.</p> <p>9 A Preprint or published?</p> <p>10 MS. THOMPSON:</p> <p>11 Q Either.</p> <p>12 A So I think the preprint came first,</p> <p>13 obviously. The expert report was available</p> <p>14 first, and then the preprint, and then just</p> <p>15 within, I think, a month and a half I got the</p> <p>16 paper. It was pretty recent.</p> <p>17 Q Is Dr. Saenz's published manuscript on</p> <p>18 your supplemental materials list?</p> <p>19 MS. CURRY:</p> <p>20 It's attached to the objections, which</p> <p>21 is Exhibit 3.</p> <p>22 MS. THOMPSON:</p> <p>23 Yeah. I -- I couldn't find my notice</p> <p>24 with objections.</p>	<p style="text-align: right;">Page 49</p> <p>1 Q If it was December, would that surprise</p> <p>2 you?</p> <p>3 MS. CURRY:</p> <p>4 Object to the form.</p> <p>5 A December of --</p> <p>6 MS. THOMPSON:</p> <p>7 Q Of '18?</p> <p>8 A That's pretty recent.</p> <p>9 Q Were you not aware that this had been</p> <p>10 put online by Health Canada prior to Dr. Saenz's</p> <p>11 deposition?</p> <p>12 A I was not.</p> <p>13 Q Did you review that 2014 letter from</p> <p>14 FDA in response to a public citizen complaint?</p> <p>15 A I am familiar with that.</p> <p>16 (DEPOSITION EXHIBIT NUMBER 5</p> <p>17 WAS MARKED FOR IDENTIFICATION.)</p> <p>18 MS. THOMPSON:</p> <p>19 Q And I'll mark that 2014 public citizen</p> <p>20 response letter from the FDA as Exhibit Number 5.</p> <p>21 Does that look like the letter that you</p> <p>22 reviewed, Dr. Birrer?</p> <p>23 A (Nods affirmatively.) I've seen that,</p> <p>24 yeah.</p>

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<p style="text-align: right;">Page 50</p> <p>1 Q And did you review the IARC Monograph 2 on Nonasbestiform Talc from 2010? 3 A I did. 4 Q And that will be Exhibit Number 6. 5 (DEPOSITION EXHIBIT NUMBER 6 6 WAS MARKED IDENTIFICATION.) 7 MS. THOMPSON: 8 Q Does that look like the document that 9 you reviewed? 10 A Yes. Yeah. I've seen that. Yep. 11 MS. THOMPSON: 12 Dawn, if you want more copies, I'm 13 happy to give -- 14 MS. CURRY: 15 I'm okay. I don't know if other 16 counsel need a copy to review. 17 MR. MIZGALA: 18 No. 19 MS. THOMPSON: 20 I think for most everything I have 21 another copy, so if there's anything you'd like 22 to see and not have to take home with you, I'm 23 happy to provide it. 24 MS. THOMPSON:</p>	<p style="text-align: right;">Page 52</p> <p>1 Q Okay. That's my question. 2 A Yes. 3 Q But it was published in December, and 4 you didn't look at it until you saw it in 5 Dr. Saenz's deposition as an exhibit; right? 6 A Correct. 7 Q Did you deem it important? 8 MS. CURRY: 9 Object to the form. 10 A Well, since it was quoted and my 11 impression was that there were people who thought 12 this was important, that necessitated me to take 13 a look at it. 14 MS. THOMPSON: 15 Q Did you think it was important? 16 MS. CURRY: 17 Object to the form. 18 A Well, after I read it, again, my sense 19 was it doesn't really sway me one more -- one way 20 or the other because they're -- they're 21 essentially re-reviewing all the data that we 22 know and coming to a different conclusion. I 23 just think they got it wrong, unfortunately. 24 MS. THOMPSON:</p>
<p style="text-align: right;">Page 51</p> <p>1 Q Did you know that the Health Canada 2 assessment was made pub- -- made available to the 3 public? 4 A Yes. 5 MS. CURRY: 6 Object to the form. 7 MS. THOMPSON: 8 Q Do you believe that the Health Canada 9 risk assessment is relevant to the topic today? 10 MS. CURRY: 11 Object to the form. 12 A It doesn't change my opinion about 13 biologic plausibility. It's a -- obviously, an 14 opinion that's based upon a lot of data that I 15 believe is reviewed by Taher, which is 16 information data that I already was aware of, so 17 it doesn't really sway me one way or the other. 18 MS. THOMPSON: 19 Q But my question was, did you deem it 20 relevant? 21 MS. CURRY: 22 Object to the form. 23 A Relevant to review. 24 MS. THOMPSON:</p>	<p style="text-align: right;">Page 53</p> <p>1 Q But you will agree that it did provide 2 an extensive review on the subject? 3 MS. CURRY: 4 Object to the form. 5 A It was, I thought, would be described 6 as extensive. 7 MS. THOMPSON: 8 Q Did you review the statement of the 9 methodology that accompanied the risk assessment? 10 A I went -- I looked through it. 11 Q I'll mark that as Exhibit 7. 12 (DEPOSITION EXHIBIT NUMBER 7 13 WAS MARKED IDENTIFICATION.) 14 MS. THOMPSON: 15 Q Is that what you saw? 16 A I didn't see it printed like this with 17 the color on it. Yeah. 18 Q And let's just look at page 2 of the 19 document titled "Weight of Evidence, General 20 Principles and Current Applications in Health 21 Canada." 22 Does number 3, Role in Risk 23 Assessments, generally outline the methodology 24 that Health Canada applied to this risk</p>

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<p style="text-align: right;">Page 54</p> <p>1 assessment?</p> <p>2 MS. CURRY:</p> <p>3 Object to the form.</p> <p>4 A Yeah. I think it's a summary of</p> <p>5 what -- of how they approached it. That's my</p> <p>6 sense. Yep.</p> <p>7 MS. THOMPSON:</p> <p>8 Q And for the risk assessment, Health</p> <p>9 Canada assumed talc or talcum products to be</p> <p>10 nonasbestiform.</p> <p>11 Is that your understanding?</p> <p>12 A Yeah. I believe that's what they</p> <p>13 focused on.</p> <p>14 Q What does nonasbestiform mean?</p> <p>15 A I'm not going to go down the line of</p> <p>16 being an expert in asbestos.</p> <p>17 Q So do you not know what it means when</p> <p>18 the talc is considered nonasbestiform?</p> <p>19 MS. CURRY:</p> <p>20 Object to the form.</p> <p>21 A I'm assuming they're addressing sort of</p> <p>22 mineral characterization of these substances.</p> <p>23 But again, I -- that's not my area of expertise.</p> <p>24 I'm not a geologist and it -- it in many ways is</p>	<p style="text-align: right;">Page 56</p> <p>1 MS. THOMPSON:</p> <p>2 Q So you're agreeing it's irrelevant what</p> <p>3 form the particles are in when --</p> <p>4 A I'm saying we don't have any data.</p> <p>5 MS. CURRY:</p> <p>6 Object to the form.</p> <p>7 You have to let her get her --</p> <p>8 THE WITNESS:</p> <p>9 Okay.</p> <p>10 MS. CURRY:</p> <p>11 -- entire question out before you</p> <p>12 answer so that the court reporter can get</p> <p>13 everything down.</p> <p>14 MS. THOMPSON:</p> <p>15 Q No data isn't the same as irrelevant,</p> <p>16 and that's my question.</p> <p>17 MS. CURRY:</p> <p>18 Object to the form.</p> <p>19 A You know, again, I don't think I can</p> <p>20 answer that "yes" or "no."</p> <p>21 MS. THOMPSON:</p> <p>22 Q Is it important whether the substance</p> <p>23 in Johnson's baby powder and Shower to Shower is</p> <p>24 in a particulate form or in a fiber form?</p>
<p style="text-align: right;">Page 55</p> <p>1 sort of irrelevant to looking at many of the</p> <p>2 studies which are just looking at talcum powder.</p> <p>3 MS. THOMPSON:</p> <p>4 Q Does it not matter to you whether that</p> <p>5 talc is in a particle or fiber -- fiber form?</p> <p>6 MS. CURRY:</p> <p>7 Object to the form.</p> <p>8 A Well, I looked at, again, extensively</p> <p>9 all the data that was addressing whether talcum</p> <p>10 powder is a risk factor or plays a role in</p> <p>11 developing ovarian cancer. It is irrelevant in</p> <p>12 that setting whether there are components in</p> <p>13 there that go from asbestiform to heavy metals to</p> <p>14 fragrance. That data would be clear from those</p> <p>15 experiments, and they're not.</p> <p>16 MS. THOMPSON:</p> <p>17 Q So is the answer that -- is it</p> <p>18 irrelevant whether the particles are in a</p> <p>19 particulate form or in a fiber form?</p> <p>20 MS. CURRY:</p> <p>21 Object to the form.</p> <p>22 A Again, I -- that -- that experiment has</p> <p>23 not been done in the -- the -- in the -- in the</p> <p>24 data that I looked at.</p>	<p style="text-align: right;">Page 57</p> <p>1 MS. CURRY:</p> <p>2 Object to the form.</p> <p>3 A I don't know.</p> <p>4 MS. THOMPSON:</p> <p>5 Q You don't know if it's important?</p> <p>6 A I don't know if it's important.</p> <p>7 Q Okay. And is part of the reason is</p> <p>8 because you're not an expert in asbestos?</p> <p>9 MS. CURRY:</p> <p>10 Object to the form.</p> <p>11 A Again, I wasn't asked to evaluate the</p> <p>12 role of asbestos in ovarian cancer. I have an</p> <p>13 opinion on that based upon some of the</p> <p>14 epidemiologic studies.</p> <p>15 But in terms of the compositional</p> <p>16 analysis of talcum powder, that is not within the</p> <p>17 area of my expertise, and the various forms of</p> <p>18 asbestos in talc in terms of mineralogy is not</p> <p>19 something that I've spent time on.</p> <p>20 But, as I pointed out before, the</p> <p>21 experiments that have been conducted address that</p> <p>22 issue, which is they're using talcum powder. If</p> <p>23 it's got a variety of substances in it, any one</p> <p>24 of which match and play a role in ovarian cancer,</p>

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<p style="text-align: right;">Page 58</p> <p>1 it would have been obvious from the data and it's</p> <p>2 not.</p> <p>3 MS. THOMPSON:</p> <p>4 Q Is it your opinion that baby powder and</p> <p>5 Shower to Shower -- and you understand those are</p> <p>6 the two products that we're here to talk about</p> <p>7 today; right?</p> <p>8 A Yes. J & J products?</p> <p>9 Q Yes.</p> <p>10 Is it your opinion that those products</p> <p>11 have been proven safe?</p> <p>12 MS. CURRY:</p> <p>13 Object to the form.</p> <p>14 A So there's no data that I know of that</p> <p>15 says they're not safe.</p> <p>16 MS. THOMPSON:</p> <p>17 Q That's different. Have they been</p> <p>18 proven safe?</p> <p>19 MS. CURRY:</p> <p>20 Object to the form.</p> <p>21 A Yes.</p> <p>22 MS. THOMPSON:</p> <p>23 Q And what data do you have as the basis</p> <p>24 for that, that they have been proven safe?</p>	<p style="text-align: right;">Page 60</p> <p>1 has it been proven unsafe, so --</p> <p>2 MR. MIZGALA:</p> <p>3 Object to the form.</p> <p>4 MS. THOMPSON:</p> <p>5 Q -- I'll ask the question again.</p> <p>6 Have these products been proven safe in</p> <p>7 your mind?</p> <p>8 MS. CURRY:</p> <p>9 Object to the form.</p> <p>10 A Again, it is -- it is an issue about</p> <p>11 trying to prove a negative. The data is there</p> <p>12 are decades of use of this, this material,</p> <p>13 perineal dusting, with no evidence, no convincing</p> <p>14 evidence that it's unsafe. I conclude that it's</p> <p>15 a safe product.</p> <p>16 MS. THOMPSON:</p> <p>17 Q Do you believe that the molecular data</p> <p>18 proves the product safe?</p> <p>19 MS. CURRY:</p> <p>20 Object to the form.</p> <p>21 A Can you define "molecular data"?</p> <p>22 MS. THOMPSON:</p> <p>23 Q The -- the studies that have been</p> <p>24 performed on talcum powder, do you believe they</p>
<p style="text-align: right;">Page 59</p> <p>1 A Again, years and years of usage with</p> <p>2 these experiments and biologic systems,</p> <p>3 epidemiologic data is basically not exposing or</p> <p>4 uncovering any definitive data that that they're</p> <p>5 unsafe.</p> <p>6 Q So you believe the epidemiological data</p> <p>7 proves the product safe?</p> <p>8 A I don't think it -- it proves that it's</p> <p>9 a risk factor.</p> <p>10 Q Is that --</p> <p>11 A You're asking -- you're asking me to</p> <p>12 prove a negative. I can't do that.</p> <p>13 Q So you're not -- you're unable to prove</p> <p>14 that it's safe because you can't prove a</p> <p>15 negative?</p> <p>16 MS. CURRY:</p> <p>17 Object to the form.</p> <p>18 MS. THOMPSON:</p> <p>19 Q Is that what you're saying?</p> <p>20 A I get -- yeah. I think -- I think the</p> <p>21 issue in front of us is: Is it unsafe? And the</p> <p>22 answer to that is there's no data for it.</p> <p>23 Q Well, the issue is what I asked you.</p> <p>24 And my question was has it been proven safe, not</p>	<p style="text-align: right;">Page 61</p> <p>1 prove that the products are safe?</p> <p>2 MS. CURRY:</p> <p>3 Object to the form.</p> <p>4 A Just repeat that once more, please.</p> <p>5 MS. THOMPSON:</p> <p>6 Q The molecular studies that have been</p> <p>7 done on talcum powder, is it your opinion that</p> <p>8 they prove that the products are safe?</p> <p>9 MS. CURRY:</p> <p>10 Object to the form.</p> <p>11 A So I refine that a bit because I don't</p> <p>12 really consider them molecular studies. They're</p> <p>13 biologic studies, and there's a difference.</p> <p>14 The biologic studies which I reviewed,</p> <p>15 which I think is the sum total that's out there,</p> <p>16 are completely unconvincing, unconvincing that</p> <p>17 talcum powder is a -- plays a role in the</p> <p>18 development of ovarian cancer.</p> <p>19 MS. THOMPSON:</p> <p>20 Q But my question was is it your belief</p> <p>21 that the biologic studies confirm that the</p> <p>22 product is safe?</p> <p>23 MS. CURRY:</p> <p>24 Object to the form.</p>

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<p>1 A Again, we're back sort of to that 2 negative. I -- I think if -- I don't think they 3 convince me at all that it's -- it's a risk or 4 that it has any biologic activity on the target 5 organ, which is the ovary. And then in the 6 context of decades of use, then I would conclude 7 that it's a safe product. 8 MS. THOMPSON: 9 Q And it's fine to say you can't 10 answer -- you can't answer the question. But I 11 need -- but I want to have an answer. 12 And that is: Is it your opinion that 13 the biologic studies show that the products are 14 safe? 15 MS. CURRY: 16 Object to the form. 17 A Yeah. I -- I think -- I think 18 certainly that -- I think we can say that the 19 biologic studies do not reveal any untoward 20 effects. It's not reliable. The experiments are 21 not reliable. And so in that context, it's a 22 safe product. 23 I mean, again, you're asking me for a 24 biologic experiment that proves something is</p>	<p>1 reviewing the assessment? 2 A I believe so, but let me just -- 3 MS. CURRY: 4 Do you have the marked Exhibit 4 there? 5 I don't think the witness actually has 6 the -- 7 Oh, I think it's in front of you here. 8 I'm just gonna grab these marked 9 exhibits for him. Thank you. 10 MS. THOMPSON: 11 I think his is the marked exhibit, 12 unless I -- 13 MS. CURRY: 14 Right. It was just in front of you. 15 MS. THOMPSON: 16 Oh, I -- yeah. 17 MS. CURRY: 18 He didn't have it. That's all. 19 MS. THOMPSON: 20 Sorry. 21 A Yeah, this -- okay. 22 Yeah. So they -- they essentially went 23 through it in that kind of algorithm. 24 MS. THOMPSON:</p>
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<p>1 safe. I don't even know how to conduct an 2 experiment like that. 3 MS. THOMPSON: 4 Q Okay. And again, you know, I can't 5 answer that -- your question -- 6 A It's okay? 7 Q -- is a fine answer. Yeah. 8 MS. CURRY: 9 Object to the form. 10 MS. THOMPSON: 11 Q Back to the weight of the evidence 12 document, it's your understanding that this is 13 the evaluation that Health Canada applied to -- 14 A That's this one? 15 Q Yeah. 16 -- to answering the -- the question of 17 whether talcum powder was a risk for the public 18 in Canada; correct? 19 MS. CURRY: 20 Object to the form. 21 A Correct. 22 MS. THOMPSON: 23 Q And they also applied a Bradford Hill 24 analysis? Is that your understanding from</p>	<p>1 Q I did not see any discussion in your 2 report of a methodology similar to this. Is that 3 right? 4 A Correct. 5 Q Did you perform a weight of the 6 evidence of the data in this case? 7 A So I approached the expert report based 8 upon my experience, both scientifically and 9 clinical. We do this -- we do this a lot, 10 actually, where we'll do a complete review of the 11 literature and then extract the information, 12 dissect it in terms of paper by paper. 13 As a scientist, we don't really weigh 14 studies in a quantitative way. We don't -- it's 15 really not like a meta-analysis where we're 16 saying, okay, this is -- this is this weight 17 versus that weight. 18 But -- but the gestalt is, if you will, 19 at the end of the day, we look at these studies 20 and say do we believe -- do we think that the 21 data and results are believable; do they -- do 22 they support the conclusions. And we do that 23 individually through all the studies. 24 And my expert report, I think, outlines</p>

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<p style="text-align: right;">Page 66</p> <p>1 that very clearly.</p> <p>2 So I guess the answer to your question</p> <p>3 is at the end of the day, the conclusion is that</p> <p>4 we don't think -- I don't think the data supports</p> <p>5 a biologic plausibility for talc versus -- talc</p> <p>6 and the -- as a role in the development of</p> <p>7 ovarian cancer. That's the sum total of all that</p> <p>8 analysis.</p> <p>9 Q Did you perform a Bradford Hill</p> <p>10 analysis, per se?</p> <p>11 A Not in the expert report. It's really</p> <p>12 focused on biologic plausibility. I'm aware of</p> <p>13 Bradford Hill. Prior depositions, we talked</p> <p>14 about the elements, and I feel like I -- I</p> <p>15 certainly understand those criteria.</p> <p>16 Q But at least in this report, you didn't</p> <p>17 apply the criteria to this subject?</p> <p>18 MS. CURRY:</p> <p>19 Object to the form.</p> <p>20 A It's really focused on biologic</p> <p>21 plausibility, which, as you know, is one</p> <p>22 component of it.</p> <p>23 MS. THOMPSON:</p> <p>24 Q Correct.</p>	<p style="text-align: right;">Page 68</p> <p>1 Q Is it a credible scientific</p> <p>2 organization?</p> <p>3 MS. CURRY:</p> <p>4 Object to the form.</p> <p>5 A I -- I think, to be fair, they -- they</p> <p>6 recognize this as a group that is careful and is</p> <p>7 invested in this. I would say, though, that</p> <p>8 they're not, as an organization, completely free</p> <p>9 of -- because of the way they're structured with</p> <p>10 WHO, completely free of outside influence or</p> <p>11 politics. That's my sense.</p> <p>12 MS. THOMPSON:</p> <p>13 Q And by outside influence and politics,</p> <p>14 where would that be coming from?</p> <p>15 A From World Health Organization, which</p> <p>16 is their sort of supervising body.</p> <p>17 Q And is it your belief that the World</p> <p>18 Health Organization is politically biased or</p> <p>19 subject to influence from outside?</p> <p>20 A Well, I think it's an organization</p> <p>21 that, by its nature, is, you know, a compendium</p> <p>22 of countries and societies. And, so, it's --</p> <p>23 let's just say it's not necessarily as sort of</p> <p>24 independent as the Academy, National Academy.</p>
<p style="text-align: right;">Page 67</p> <p>1 And you reviewed that IARC 2010</p> <p>2 document that we've marked as an exhibit; right.</p> <p>3 A This is when it was labeled as 2B;</p> <p>4 right?</p> <p>5 Q Yes.</p> <p>6 And -- and this -- well, this monograph</p> <p>7 was published in 2010; right?</p> <p>8 A Correct.</p> <p>9 Q Is it your understanding that it</p> <p>10 considered literature up to 2006? Correct?</p> <p>11 A Sounds about right, yes.</p> <p>12 Q What is IARC?</p> <p>13 A Well, it's an international agency for</p> <p>14 research on cancer. Part of what they -- their</p> <p>15 responsibility is is to look at environmental</p> <p>16 risks for -- and -- and to sort of attempt to</p> <p>17 quantify them, identify them and quantify them</p> <p>18 for the development of cancer.</p> <p>19 Q Is it generally thought to be a</p> <p>20 reputable scientific organization?</p> <p>21 MS. CURRY:</p> <p>22 Object to the form.</p> <p>23 A How do you define "reputable"?</p> <p>24 MS. THOMPSON</p>	<p style="text-align: right;">Page 69</p> <p>1 Q And by that you mean the National</p> <p>2 Academy of Science and Medicine Engineering, now</p> <p>3 titled?</p> <p>4 A Yes.</p> <p>5 Q Okay. And I believe we talked about</p> <p>6 before this --</p> <p>7 A Uh-huh.</p> <p>8 Q -- this monograph applies to talc not</p> <p>9 containing asbestiform fibers, but that is not</p> <p>10 your area of expertise; correct?</p> <p>11 MS. CURRY:</p> <p>12 Object to the form.</p> <p>13 A Correct.</p> <p>14 MS. THOMPSON:</p> <p>15 Q And you are aware that there's a</p> <p>16 different IARC monograph published in 2012 that</p> <p>17 would cover talc containing asbestos or talc</p> <p>18 containing asbestiform fibers; correct?</p> <p>19 A I don't think I've seen that.</p> <p>20 Q That would be 2012, the 100C. I</p> <p>21 believe it's on your --</p> <p>22 A Is it?</p> <p>23 Q -- reliance list.</p> <p>24 A Do you have a copy?</p>

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<p>1 Q Yeah. It's number 77.</p> <p>2 A 77.</p> <p>3 Q Arsenic, Metals, Fibers and Dust?</p> <p>4 A Oh, I think I -- I'm sorry. That's</p> <p>5 coming back to me. It was a small -- yeah.</p> <p>6 Q And did you -- did you review that IARC</p> <p>7 monograph?</p> <p>8 A Yeah. There was a -- what -- what</p> <p>9 I looked at was a subset of the entire document.</p> <p>10 Yeah.</p> <p>11 Q Did you look at the section with</p> <p>12 asbestos?</p> <p>13 MS. CURRY:</p> <p>14 Object to the form.</p> <p>15 A I believe so, yeah.</p> <p>16 MS. THOMPSON:</p> <p>17 Q Did you look at the section with heavy</p> <p>18 metals?</p> <p>19 A No.</p> <p>20 Q Are you aware that that document, 2012,</p> <p>21 100C, includes all forms of asbestos and talc</p> <p>22 containing asbestiform fibers?</p> <p>23 A That sounds correct.</p> <p>24 Q But you're not sure about that today?</p>	<p>1 Object to the form.</p> <p>2 A It's detailed.</p> <p>3 MS. THOMPSON:</p> <p>4 Q Going to the FDA response letter, at</p> <p>5 least by volume, would you agree that this FDA</p> <p>6 letter is a less extensive review?</p> <p>7 MS. CURRY:</p> <p>8 Object to the form.</p> <p>9 A Less pages.</p> <p>10 MS. THOMPSON:</p> <p>11 Q That's kind of what I was getting at.</p> <p>12 How about references?</p> <p>13 A Yeah.</p> <p>14 Q So, essentially, the FDA response</p> <p>15 letter in 2014 does not include a description of</p> <p>16 the methodology or an extensive reference list.</p> <p>17 Is a that fair --</p> <p>18 MS. CURRY:</p> <p>19 Object to the form.</p> <p>20 MS. THOMPSON:</p> <p>21 Q -- statement?</p> <p>22 A Well, I -- again, I think a little bit</p> <p>23 you're comparing apples and oranges in the sense</p> <p>24 that the purpose for these documents is somewhat</p>
Page 71	Page 73
<p>1 MS. CURRY:</p> <p>2 Object to the form.</p> <p>3 A Well, as I said, I'm not a asbestos</p> <p>4 expert. But that -- that IARC volume is focused</p> <p>5 on fibers, so that makes sense.</p> <p>6 MS. THOMPSON:</p> <p>7 Q And have you reviewed the preamble to</p> <p>8 the IARC monographs? It's included in --</p> <p>9 A Yeah.</p> <p>10 Q -- in exhibit --</p> <p>11 A I looked through it.</p> <p>12 Q Okay.</p> <p>13 A It's voluminous.</p> <p>14 Q And does that describe the -- the</p> <p>15 methodology that IARC applies when it's looking</p> <p>16 to determine whether a substance is carcinogenic</p> <p>17 or not?</p> <p>18 A Yes. It's a list of all the</p> <p>19 participants, the general principles, the</p> <p>20 methodology.</p> <p>21 Q And you would agree, similar to Health</p> <p>22 Canada, that that methodology is extensive as</p> <p>23 well?</p> <p>24 MS. CURRY:</p>	<p>1 different in that this is a letter from the FDA</p> <p>2 in response to a -- I think it was a citizen's</p> <p>3 petition. They're not gonna give -- they're not</p> <p>4 gonna send this back to a citizen's petition</p> <p>5 because I think the citizen's petition would be</p> <p>6 insulted because they're not going to be able to</p> <p>7 read it. It's more of a letter than the -- what</p> <p>8 their opinion is.</p> <p>9 Oh. Sorry.</p> <p>10 Q And you're referring to that IARC --</p> <p>11 A Yeah.</p> <p>12 Q -- 2010 monograph. Yeah.</p> <p>13 A Yeah.</p> <p>14 Q Fair enough.</p> <p>15 However, you would consider the FDA a</p> <p>16 credible source?</p> <p>17 A Yes.</p> <p>18 Q Let's look at your CV. And you have</p> <p>19 been a prolific researcher. Would you agree?</p> <p>20 A I survive.</p> <p>21 Q I -- I think there are approximately</p> <p>22 400 published papers. Is that close?</p> <p>23 A Correct.</p> <p>24 Q You have a lot of coauthors on these</p>

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<p>1 papers. Am I right?</p> <p>2 A Correct.</p> <p>3 Q On some, you're the lead author;</p> <p>4 correct?</p> <p>5 A Correct.</p> <p>6 Q What does the role of lead author</p> <p>7 usually entail?</p> <p>8 MS. CURRY:</p> <p>9 Object to the form.</p> <p>10 A So let me -- let me step back and</p> <p>11 define that. I would say anchor positions.</p> <p>12 MS. THOMPSON:</p> <p>13 Q Okay.</p> <p>14 A So first author is usually the person</p> <p>15 who has done most of the work. And, it</p> <p>16 actually -- my first authorship positions have</p> <p>17 sort of faded with time because I take the other</p> <p>18 anchor position, which is the senior author,</p> <p>19 where you're providing guidance, mentorship, and</p> <p>20 then you -- you ultimately are responsible for</p> <p>21 the quality of the paper.</p> <p>22 Q And -- and that --</p> <p>23 A Yeah.</p> <p>24 Q -- that person is -- is often listed</p>	<p>1 A No. I think OCAC is a lot like that.</p> <p>2 MS. THOMPSON:</p> <p>3 Q They're providing tissue samples or are</p> <p>4 they providing expertise?</p> <p>5 A Well, OCAC is the consortium, so</p> <p>6 it's -- it's composed of all of those</p> <p>7 institutions. And those institutions are</p> <p>8 providing specimens. And then the authors from</p> <p>9 those institutions end up on the paper.</p> <p>10 Q How are the authors of the consortium's</p> <p>11 publications selected?</p> <p>12 MS. CURRY:</p> <p>13 Object to the form.</p> <p>14 A Specific in GWAS or in general?</p> <p>15 MS. THOMPSON:</p> <p>16 Q In OCAC.</p> <p>17 A OCAC. Well, I'm not sure I can quote</p> <p>18 you OCAC rules, but the general guidelines would</p> <p>19 be that from every institution that participated,</p> <p>20 there'd be a primary author. If -- if there was</p> <p>21 somebody else at the institution who specifically</p> <p>22 did something important for that paper, they</p> <p>23 might take two authors. But usually there's a</p> <p>24 limit because you just -- OCAC, I believe, has --</p>
Page 75	Page 77
<p>1 last. Is that right?</p> <p>2 A That's right.</p> <p>3 Q Okay. And can I assume that the</p> <p>4 authors in the middle have varying roles but all</p> <p>5 participate in the preparation of the manuscript</p> <p>6 in some sense?</p> <p>7 A Right. I mean, it becomes -- you</p> <p>8 probably can guess -- somewhat problematic when</p> <p>9 you look at GY studies when there are almost more</p> <p>10 authors than specimens. So the idea there is</p> <p>11 that the individuals in -- in between are still</p> <p>12 contributing to the paper. They're -- they may</p> <p>13 be providing specimens.</p> <p>14 Q And I believe in GWAS, the -- the</p> <p>15 recruitment for GWAS are researchers that can</p> <p>16 provide tissue specimens for the group that's</p> <p>17 analyzing them. Is that a fair --</p> <p>18 A It's a big point. It's -- it's a big</p> <p>19 part of it. Yeah.</p> <p>20 Q And you'd agree that that's different</p> <p>21 from the consortium that we discussed earlier,</p> <p>22 that OCAC consortium; right?</p> <p>23 MS. CURRY:</p> <p>24 Object to the form.</p>	<p>1 I'm guessing -- 50 to maybe even 100</p> <p>2 institutions. So if you were to allow unlimited</p> <p>3 authors, it would be unmanageable.</p> <p>4 Q Would the authors typically be</p> <p>5 considered to have expertise in the particular</p> <p>6 area that they're publishing in?</p> <p>7 A Yes.</p> <p>8 Q Would they typically have previous</p> <p>9 scholarly work or publications?</p> <p>10 MS. CURRY:</p> <p>11 Object to the form.</p> <p>12 A Usually.</p> <p>13 MS. THOMPSON:</p> <p>14 Q Would they typically have a -- a good</p> <p>15 reputation in the scientific or medical</p> <p>16 community?</p> <p>17 MS. CURRY:</p> <p>18 Object to the form.</p> <p>19 A I hope so.</p> <p>20 MS. THOMPSON:</p> <p>21 Q Would they typically be knowledgeable</p> <p>22 in that respective field that they're called upon</p> <p>23 to contribute to the --</p> <p>24 MS. CURRY:</p>

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<p style="text-align: right;">Page 78</p> <p>1 Object to the form.</p> <p>2 A Yeah. I mean, I think it would be</p> <p>3 very -- again, these GWAS studies -- I'm sorry --</p> <p>4 the GWAS studies are in some ways really unique</p> <p>5 in that there's so many authors. There may be</p> <p>6 individuals in that list who -- who while they're</p> <p>7 ovarian cancer researchers, they could be fairly</p> <p>8 junior, and they may have just provided some</p> <p>9 specimens. Yeah.</p> <p>10 MS. THOMPSON:</p> <p>11 Q Yeah. And I'm not as interested in the</p> <p>12 GWAS because they do have, you know, a whole</p> <p>13 number.</p> <p>14 A Yeah.</p> <p>15 Q But I'm thinking more of the Australian</p> <p>16 consortium, the OCAC, the -- the other ones where</p> <p>17 it looks, at least by appearance, that you're --</p> <p>18 the authors are chosen because they're experts</p> <p>19 in -- in a particular area. For example,</p> <p>20 epidemiology. Would you agree with that</p> <p>21 statement?</p> <p>22 MS. CURRY:</p> <p>23 Object to the form.</p> <p>24 A I think that's true -- I think that's</p>	<p style="text-align: right;">Page 80</p> <p>1 of careful thought.</p> <p>2 MS. THOMPSON:</p> <p>3 Q And -- and I'd assume they'd be</p> <p>4 qualified in their area of expertise for the same</p> <p>5 reason, or else you wouldn't choose them. Right?</p> <p>6 A It would be hard for them to contribute</p> <p>7 in a meaningful way if they don't know what</p> <p>8 they're doing.</p> <p>9 Q Okay. Looking at your CV, are there</p> <p>10 any coauthors that you can identify that you</p> <p>11 would not regard as qualified in their respective</p> <p>12 fields?</p> <p>13 A I'm not gonna be able to answer that.</p> <p>14 I've got 400 publications and probably several</p> <p>15 thousand authors.</p> <p>16 Q So do you think there would be some</p> <p>17 that you could identify as not being credible?</p> <p>18 A Not that I know of.</p> <p>19 MS. CURRY:</p> <p>20 Object to the form.</p> <p>21 A Again, this is realtime, so if we go</p> <p>22 back to my Ph.D., which was on the measles virus</p> <p>23 back when I was a young lad, I don't know that</p> <p>24 field anymore, and I don't know what those</p>
<p style="text-align: right;">Page 79</p> <p>1 true as a -- as general guideline, yeah.</p> <p>2 MS. THOMPSON:</p> <p>3 Q And would the same be true for a paper</p> <p>4 that you're publishing? Would you look for</p> <p>5 coauthors -- either as an anchor or a senior,</p> <p>6 would you look for coauthors that are credible?</p> <p>7 A Well, you know, when you do these</p> <p>8 experiments, you're not really out looking for</p> <p>9 authors. You're doing the experiments, and the</p> <p>10 people who do them, help you design a project,</p> <p>11 deserve authorship. Those are the guidelines.</p> <p>12 And if you're asking would I put</p> <p>13 somebody who I thought was not credible on an</p> <p>14 author list, I'd be very bothered by that. But</p> <p>15 you'd have to define what "credible" means.</p> <p>16 Q Yeah. So I guess rather than choosing</p> <p>17 someone as a coauthor, I should have rephrased</p> <p>18 that. Choosing someone to work on a project that</p> <p>19 would later be published, you can assume that</p> <p>20 person would be credible; correct?</p> <p>21 MS. CURRY:</p> <p>22 Object to the form.</p> <p>23 A Yeah. I choose my collaborators, like</p> <p>24 others, other scientists, with a certain amount</p>	<p style="text-align: right;">Page 81</p> <p>1 individuals have done.</p> <p>2 It's a realtime process. Sometimes</p> <p>3 individuals who seem to be very, very good</p> <p>4 scientists later on in life will get involved in</p> <p>5 scientific misconduct. That may not have been at</p> <p>6 all relevant for when you put that person on your</p> <p>7 paper.</p> <p>8 (DEPOSITION EXHIBIT NUMBER 8</p> <p>9 WAS MARKED IDENTIFICATION.)</p> <p>10 MS. THOMPSON:</p> <p>11 Q I'm gonna just give you a list of some</p> <p>12 coauthors that I pulled off your CV. And would</p> <p>13 you look at that list?</p> <p>14 A Uh-huh.</p> <p>15 Q I narrowed it down from a couple</p> <p>16 thousand to a more manageable number. Are there</p> <p>17 any names on that list that you could identify as</p> <p>18 not being credible?</p> <p>19 MS. CURRY:</p> <p>20 Object to the form.</p> <p>21 MS. THOMPSON:</p> <p>22 Q And that list is marked as Exhibit --</p> <p>23 Dr. Birrer, can you --</p> <p>24 A 8.</p>

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<p style="text-align: right;">Page 82</p> <p>1 Q -- 8. 2 A So I would say of this list, 3 probably -- I'm estimating -- about 20 percent of 4 these people, I'm -- I'm not sure I quite 5 remember what paper they're on. But the rest of 6 them I know because they're high profile. I 7 don't see anybody here that I would say is not a 8 good scientist. 9 Q And qualified in their respective 10 areas? 11 A Yes. 12 MS. CURRY: 13 Object to the form. 14 MS. THOMPSON: 15 Q And some -- at least some on the list 16 you published with multiple times. Is that fair 17 to say? 18 A Yeah. 19 Q Dr. Birrer, throughout your report you, 20 at least at times, used the term "talc." What 21 are you referring to when you say talc? 22 A So there's two levels of relevance 23 here. One is for epidemiologic studies or 24 studies that were -- that were conducted. A</p>	<p style="text-align: right;">Page 84</p> <p>1 sense is they command the market. But I'm not -- 2 I'm not in the supermarket a lot. 3 Q And not in the baby powder section? 4 A No. 5 Q And what is contained in the 6 Johnson's -- in Johnson's baby powder, to your 7 understanding? 8 MS. CURRY: 9 Object to the form. 10 A Talc. And I know that's an issue 11 that's come up in terms of are there other 12 things. I mean, clearly there are other things 13 that -- the product smells nice, so there must be 14 some fragrance. 15 MS. THOMPSON: 16 Q Okay. 17 A But I don't know of any -- first of 18 all, I don't -- that's not my area of expertise. 19 I've certainly never conducted any experiments 20 and tried to figure out what's in it and -- and 21 wouldn't consider myself an expert in the whole 22 mineralogy issue. 23 Q So that would be talc, the mineral. Do 24 you have an opinion as to whether there is a such</p>
<p style="text-align: right;">Page 83</p> <p>1 subset of the -- of the studies that were 2 conducted in the lab were actually dealing with 3 talcum powder. 4 But there are experiments in particular 5 where individuals are using sigma-produced talc. 6 So it's -- it's -- it's a bit of a mixture. But 7 I think, in particular in the epi studies, a lot 8 of them are just okay to use powder. 9 Q So to -- to the extent both of us can, 10 we can try to say whether we're referring to 11 talcum powder or talc, as you described, so 12 let's -- let's both try to do that, to the extent 13 possible, because it can get confusing. 14 A I completely concur. 15 Q Okay. Okay. I'm glad we agree on 16 that. 17 Do you know what Johnson & Johnson's 18 market share of the talcum powder product has 19 been over the years? 20 A I don't. 21 Q If I told you it was 60 to 70 percent, 22 would you have any basis to disagree with that 23 number? 24 A I actually wouldn't, because I -- my</p>	<p style="text-align: right;">Page 85</p> <p>1 thing as pure talc? 2 MS. CURRY: 3 Object to the form. 4 A You know, my -- you know, my sense is 5 in that some of the experiments where this 6 product is actually bought not cosmetically, but 7 I've seen references to sigma-produced talc, that 8 that's a -- that's a purified form of it. 9 MS. THOMPSON: 10 Q And, so, by pure -- purified form, you 11 would mean that it does not con- -- contain 12 impurities; correct? 13 A It would not contain something else. 14 Q Would you consider it pure if it 15 contained talc fibers? 16 MS. CURRY: 17 Object to the form. 18 A I don't -- I don't think I can answer 19 that. 20 MS. THOMPSON: 21 Q So no opinion on -- on that issue. 22 A Yeah. 23 Q Are you familiar with the various 24 grades of talc?</p>

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<p style="text-align: right;">Page 86</p> <p>1 A No.</p> <p>2 Q Do you have any knowledge regarding the</p> <p>3 particle size of Johnson's baby powder or Shower</p> <p>4 to Shower?</p> <p>5 A Again, that's a little bit outside my</p> <p>6 area of expertise. My understanding is, you</p> <p>7 know, talc ranges from 10 microns to larger</p> <p>8 sizes. But it's not something I systematically</p> <p>9 explored. Even the expert reports here that</p> <p>10 focused on the mineralogy, I looked at it but not</p> <p>11 in any great detail.</p> <p>12 Q And if you were told that there are</p> <p>13 also smaller particles than 10 microns, that</p> <p>14 wouldn't surprise you?</p> <p>15 A I think there's a range.</p> <p>16 Q Fair enough.</p> <p>17 A I don't know how -- you know, again, I</p> <p>18 know there's references to ultrafine, et cetera,</p> <p>19 et cetera. I don't have definitive knowledge or</p> <p>20 data that that is true.</p> <p>21 Q Okay. But, as far as you know, the</p> <p>22 particle size is -- is mixed?</p> <p>23 A Uh-huh.</p> <p>24 Q It's not a standard size like you might</p>	<p style="text-align: right;">Page 88</p> <p>1 Q It was the -- it was a report that</p> <p>2 addressed the fragrance chemicals in talcum</p> <p>3 powder. Do you remember seeing that? I don't</p> <p>4 remember whether it's on your list. Oh.</p> <p>5 A Is that plaintiff?</p> <p>6 Q You don't have Dr. Crowley's report.</p> <p>7 A Yeah.</p> <p>8 Q Did you know if there was a -- an</p> <p>9 expert report that specifically addressed the</p> <p>10 fragrance -- fragrance chemical presence in baby</p> <p>11 powder?</p> <p>12 A Not that I know of.</p> <p>13 Q So I -- I can assume that you don't</p> <p>14 know why you weren't provided Dr. Crowley's</p> <p>15 report?</p> <p>16 MS. CURRY:</p> <p>17 Object to the form.</p> <p>18 A It's not on my list.</p> <p>19 MS. THOMPSON:</p> <p>20 Q Did you ask if anyone had looked at the</p> <p>21 actual chemicals in baby powder?</p> <p>22 A I didn't specifically go through that,</p> <p>23 no.</p> <p>24 Q It -- is it important for you to know</p>
<p style="text-align: right;">Page 87</p> <p>1 see, for example, in a pleurodesis talc?</p> <p>2 MS. CURRY:</p> <p>3 Object to the form.</p> <p>4 A I don't -- I can't say that.</p> <p>5 MS. THOMPSON:</p> <p>6 Q Okay.</p> <p>7 A But based on my rudimentary</p> <p>8 understanding of mineralogy here, that there's a</p> <p>9 range.</p> <p>10 Q Have you ever looked at the label on a</p> <p>11 bottle of baby powder?</p> <p>12 A I don't recall that.</p> <p>13 Q So you don't know what would be listed</p> <p>14 on the label?</p> <p>15 A No.</p> <p>16 Q But you're assuming it has some kind of</p> <p>17 fragrances in it?</p> <p>18 A I think that's a safe assumption. I</p> <p>19 have smelled it.</p> <p>20 Q Haven't we all.</p> <p>21 Did you read Dr. Crowley's report?</p> <p>22 Do you remember Dr. Crowley's report?</p> <p>23 A That's not coming to mind. Can -- do</p> <p>24 you have it?</p>	<p style="text-align: right;">Page 89</p> <p>1 the quality of talcum powder?</p> <p>2 MS. CURRY:</p> <p>3 Object to the form.</p> <p>4 A And how do you define "quality"?</p> <p>5 MS. THOMPSON:</p> <p>6 Q I -- I define "quality" as the absence</p> <p>7 of the amount and types of impurities.</p> <p>8 MS. CURRY:</p> <p>9 Object to the form.</p> <p>10 A How do you define "impurities"?</p> <p>11 MS. THOMPSON:</p> <p>12 Q Something that's not pure talc.</p> <p>13 A Okay. Again, I -- I'll come back to</p> <p>14 this theme. I think -- I didn't go down that</p> <p>15 road. It's not my area of expertise. But, more</p> <p>16 importantly, I was asked to sort of review the</p> <p>17 total data that suggested there might be a role</p> <p>18 for talc in ovarian cancer, regard- -- talcum</p> <p>19 powder, regardless of what's in it.</p> <p>20 So in that context, impurities,</p> <p>21 fragrance, heavy metals, it doesn't matter. We</p> <p>22 would see the data. So I felt pretty comfortable</p> <p>23 that that's the -- that's the important theme for</p> <p>24 my job.</p>

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<p style="text-align: right;">Page 90</p> <p>1 Q Is it important for you to know the</p> <p>2 min- -- mineral content of a talcum powder</p> <p>3 product if you are intending to assess its</p> <p>4 potential health effects?</p> <p>5 MS. CURRY:</p> <p>6 Object to the form.</p> <p>7 A Would you just repeat that, please?</p> <p>8 MS. THOMPSON:</p> <p>9 Q Is it important to know the mineral</p> <p>10 content of a talcum powder product if you are</p> <p>11 intending to assess its potential health effects?</p> <p>12 MS. CURRY:</p> <p>13 Object to the form.</p> <p>14 A You know, again, I think in terms of</p> <p>15 reviewing the literature, no. I mean, it's</p> <p>16 talcum and it's talcum powder. It's a</p> <p>17 representative of what's on the market.</p> <p>18 So regardless of what's there or not,</p> <p>19 even from a mineral standpoint, we can make a</p> <p>20 judgment as to whether that's providing data that</p> <p>21 supports whether it's a risk factor or biologic</p> <p>22 plausibility for a role in development of ovarian</p> <p>23 cancer.</p> <p>24 MS. THOMPSON:</p>	<p style="text-align: right;">Page 92</p> <p>1 MS. THOMPSON:</p> <p>2 Q For a potential health effect.</p> <p>3 MS. CURRY:</p> <p>4 Object to the form.</p> <p>5 A There's no data for that. I can't</p> <p>6 develop a mechanism when, in fact, there's no</p> <p>7 biologic plausibility for talcum powder in a role</p> <p>8 of ovarian cancer.</p> <p>9 MS. THOMPSON:</p> <p>10 Q Well, it sounds like what you're saying</p> <p>11 is if you decide that talcum powder doesn't cause</p> <p>12 ovarian cancer, then there's no reason to even</p> <p>13 look at whether there's a plausible mechanism or</p> <p>14 not.</p> <p>15 MS. CURRY:</p> <p>16 Object to the form.</p> <p>17 MS. THOMPSON:</p> <p>18 Q Is that --</p> <p>19 A Well, I'm not sure what mechanism we're</p> <p>20 looking at. We're looking at a mechanism that an</p> <p>21 agent doesn't cause cancer? That does -- makes</p> <p>22 no sense to me.</p> <p>23 Q We're looking at what a mechanism could</p> <p>24 be if it could cause cancer, as a hypothetical.</p>
<p style="text-align: right;">Page 91</p> <p>1 Q So even in your determination of</p> <p>2 whether a biologic mechanism is plausible or not,</p> <p>3 it doesn't matter what the mineral content of the</p> <p>4 baby powder is?</p> <p>5 MS. CURRY:</p> <p>6 Object to the form.</p> <p>7 A As long as that baby powder's been</p> <p>8 tested in that experiment, it doesn't matter.</p> <p>9 MS. THOMPSON:</p> <p>10 Q And that goes for whether the baby</p> <p>11 powder contains asbestos?</p> <p>12 A Well, again, I -- I think if it</p> <p>13 contained asbestos, that would show a signal in</p> <p>14 those experiments. Now, we would see it. We may</p> <p>15 not know it's related to asbestos, fragrance or</p> <p>16 whatever, but the experiments would be</p> <p>17 reproducible and dispositive. And in my</p> <p>18 experience, they're not.</p> <p>19 Q But the question is, does that -- would</p> <p>20 that explain a mechanism if there's asbestos in</p> <p>21 the baby powder?</p> <p>22 MS. CURRY:</p> <p>23 Object to the form.</p> <p>24 A Mechanism for what?</p>	<p style="text-align: right;">Page 93</p> <p>1 MS. CURRY:</p> <p>2 Object to the form.</p> <p>3 A No. I -- a mechanism for a</p> <p>4 hypothetical. I -- you know, again, that -- we</p> <p>5 don't need the hypothetical. We've tested talcum</p> <p>6 in those experiments. There's no data to support</p> <p>7 biologic plausibility. So why are -- why would</p> <p>8 we be trying to think about a hypothetical</p> <p>9 component to produce a mechanism for a biologic</p> <p>10 activity that we haven't seen?</p> <p>11 MS. THOMPSON:</p> <p>12 Q What experiments are you referring to?</p> <p>13 A I would say primarily the ones that are</p> <p>14 in my expert report. That really is a sum- --</p> <p>15 Q Which experiments in your report? We</p> <p>16 can go through your report if you want.</p> <p>17 A I'm -- yeah.</p> <p>18 Q I'm looking for the experiments that</p> <p>19 show that there's no biologic effect.</p> <p>20 A So Buz'Zard is one that frequently --</p> <p>21 Q And is it your opinion that Buz'Zard</p> <p>22 shows no biologic effect?</p> <p>23 A There's nothing in that paper that's</p> <p>24 reliable in terms of showing biologic</p>

24 (Pages 90 to 93)

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<p style="text-align: right;">Page 94</p> <p>1 plausibility.</p> <p>2 Q And we'll get to the others.</p> <p>3 So you're referring to --</p> <p>4 A Yes.</p> <p>5 Q -- Buz'Zard, Shukla?</p> <p>6 A Shukla. Just hang on. Yeah.</p> <p>7 Buz'Zard, Shukla and Hamilton.</p> <p>8 Q And I'm going to assume you include</p> <p>9 Dr. Saed in that?</p> <p>10 A Correct.</p> <p>11 Q Although we're going to get into more</p> <p>12 detail in that later.</p> <p>13 A Exactly.</p> <p>14 Q And you're aware of the other animal</p> <p>15 studies that show inflammatory effects; right?</p> <p>16 MS. CURRY:</p> <p>17 Object to the form.</p> <p>18 A You have to go through those and define</p> <p>19 that.</p> <p>20 MS. THOMPSON:</p> <p>21 Q Okay.</p> <p>22 A Because it's pretty broad literature.</p> <p>23 You're assuming -- you're referring to</p> <p>24 Keskin?</p>	<p style="text-align: right;">Page 96</p> <p>1 What is your understanding of how these</p> <p>2 products are used by women?</p> <p>3 MS. CURRY:</p> <p>4 Object to the form.</p> <p>5 A Baby powder?</p> <p>6 MS. THOMPSON:</p> <p>7 Q And -- and we're talking about, at</p> <p>8 least for these cases, in the perineal area.</p> <p>9 A Yeah.</p> <p>10 Q Do you have any knowledge from</p> <p>11 conversations with women or literature or any</p> <p>12 other source as to how it's applied, whether it's</p> <p>13 standing, lying down, in the underwear, on a</p> <p>14 sanitary napkin, shaken into hands? Did you have</p> <p>15 any understanding of -- of those issues?</p> <p>16 MS. CURRY:</p> <p>17 Object to the form.</p> <p>18 A I would say not a systematic, shall we</p> <p>19 say, meta-analysis of baby powder use. I</p> <p>20 certainly, over years in the clinic, am familiar</p> <p>21 with women who use baby powder. You know, my</p> <p>22 sense is that most dust the perineum usually</p> <p>23 standing up. I -- but again, I can't say that's</p> <p>24 a scientific evaluation. I have some experience</p>
<p style="text-align: right;">Page 95</p> <p>1 Q There are studies going back to the</p> <p>2 '40s and '50s with intraperitoneal inflammatory</p> <p>3 effects with -- in the presence of talc.</p> <p>4 You're aware of those?</p> <p>5 MS. CURRY:</p> <p>6 Object to the form.</p> <p>7 A There is a big literature.</p> <p>8 MS. THOMPSON:</p> <p>9 Q And understanding that there are</p> <p>10 different histologic subtypes of epithelial</p> <p>11 ovarian cancer, can we agree that if one of us</p> <p>12 refers to ovarian cancer in a general sense, that</p> <p>13 we're referring to epithelial ovarian cancer?</p> <p>14 A I would not include germ -- you know,</p> <p>15 germ cell tumors in this.</p> <p>16 Q Stromal -- we're excluding stromal --</p> <p>17 A And stromal, yeah. It's epithelial,</p> <p>18 correct.</p> <p>19 Q Okay. So we're on the same page there?</p> <p>20 A With -- with the caveat being, and we</p> <p>21 do discuss this in the report about -- even</p> <p>22 within the epithelial component, we now realize</p> <p>23 there are different types of tumors.</p> <p>24 Q Understood.</p>	<p style="text-align: right;">Page 97</p> <p>1 with my wife. So I -- I -- it's a certain --</p> <p>2 some general concept of how it's done, yeah.</p> <p>3 MS. THOMPSON:</p> <p>4 Q Would you agree, at least, that, for</p> <p>5 most women, it would be applied in a -- in a</p> <p>6 habitual manner?</p> <p>7 MS. CURRY:</p> <p>8 Object to the form.</p> <p>9 A Yeah, I think it's important to define</p> <p>10 that. It would certainly be repetitive. Is it</p> <p>11 something -- you know, habitual sounds to me</p> <p>12 like -- almost like an addict. And I don't -- I</p> <p>13 don't think that's the case.</p> <p>14 MS. THOMPSON:</p> <p>15 Q No. I didn't mean it -- mean in that</p> <p>16 term.</p> <p>17 I meant that it's -- and this has been</p> <p>18 reported in the literature, I believe you're</p> <p>19 aware --</p> <p>20 A Uh-huh.</p> <p>21 Q -- that most women do it the same way</p> <p>22 every day or whatever schedule they're on.</p> <p>23 MS. CURRY:</p> <p>24 Object to the form.</p>

25 (Pages 94 to 97)

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<p style="text-align: right;">Page 98</p> <p>1 A I would think that there'd be some 2 consistency on that. I -- I will say this 3 parenthetically, you may get to it later on, but 4 I do think, based on what we're just discussing, 5 it's very hard to -- it's very hard to quantify 6 amount of use. I really do. 7 MS. THOMPSON: 8 Q And I think we will get to that. 9 A Okay. 10 Q But -- but -- so it's hard to quantify 11 how much a woman is using on any given 12 application; correct? 13 A (Nods affirmatively.) 14 Q And it's hard -- 15 MS. CURRY: 16 You have to say "yes" or "no" versus 17 head shakes because the court reporter will not 18 be able to get that down. 19 A It says "nods affirmatively." 20 Yes. 21 MS. CURRY: 22 She was able to in that instance. I 23 stand corrected, but for -- 24 THE WITNESS:</p>	<p style="text-align: right;">Page 100</p> <p>1 be true for a number of environmental 2 exposures -- 3 MS. CURRY: 4 Object to the form. 5 MS. THOMPSON: 6 Q -- that difficulty in quantifying how 7 much a particular individual is exposed to? 8 A Well, you'd have to give me some 9 examples on that. I mean, I think for cigarette 10 smoke, it actually is quite quantifiable. 11 Q Cigarette smoke, I agree. 12 How about a household or domestic 13 exposure to asbestos, for example? 14 A I guess you could quantify the amount 15 of asbestos-containing material in the house, 16 but -- 17 Q How about a spouse coming home from 18 occupational exposure? 19 A Yeah. It would be a challenge. 20 Q How about chemicals in water source? 21 A That should be measurable. 22 Q Over time? 23 A Multiple samples. 24 Q How about --</p>
<p style="text-align: right;">Page 99</p> <p>1 She's very good. 2 MS. THOMPSON: 3 Q And -- and if there were talc that 4 reached the vagina or the upper genital tract, it 5 would be hard to quantify how much that would be; 6 right? 7 A Yes. 8 Q But you'll have to agree, but -- that 9 not being able to quantify it isn't a reason not 10 to study the issue. Right? 11 MS. CURRY: 12 Object to the form. 13 A I think that's a fair statement in 14 that, you know, if it's important, you need to do 15 it. I just think that, for the reasons you just 16 said, quantifying it is -- is difficult, not only 17 in individual applications, how much actually 18 would get where, but this longitudinal issue. 19 While I think there's some consistency, do women 20 use it for a while and then stop using it and how 21 often do they change? I think there's a whole 22 issue on that, too. 23 MS. THOMPSON: 24 Q And wouldn't you agree that that would</p>	<p style="text-align: right;">Page 101</p> <p>1 A And -- and potentially even the 2 patient. 3 Q How about exposure to a pesticide? 4 A Yeah. That would be more of a 5 challenge. Yeah. 6 Q So there's certainly other -- 7 A Some variability. 8 Q -- other situations where it's 9 challenging to quantify the exposure to an 10 individual over time. 11 MS. CURRY: 12 Object to the form. 13 A Yes. 14 MS. THOMPSON: 15 Q Other than a literature or document 16 review, you -- I think I asked you this before 17 but I'm gonna just ask it again since it's in my 18 outline here. 19 Other than a literature and document 20 review, have you done any research on talcum 21 powder and ovarian cancer? 22 A No. 23 Q And that would include in vitro 24 research and in vivo; correct?</p>

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<p>1 A Correct.</p> <p>2 Q And you've never published an article</p> <p>3 on talcum powder and ovarian cancer. Is that</p> <p>4 correct?</p> <p>5 A No.</p> <p>6 Q Have you ever given a talk on talcum</p> <p>7 powder and ovarian cancer?</p> <p>8 A No.</p> <p>9 Q Have you discussed your opinions in</p> <p>10 this case with anyone?</p> <p>11 A No, other than counsel.</p> <p>12 Q No colleagues?</p> <p>13 A No.</p> <p>14 Q Did you attend the recent SGO</p> <p>15 conference in Hawaii?</p> <p>16 A Hawaii's a nice place. I did.</p> <p>17 Q Did you discuss talcum powder with any</p> <p>18 of your colleagues at the meeting?</p> <p>19 A I'd never been there before.</p> <p>20 I did not.</p> <p>21 Q Do you know Liz Swisher?</p> <p>22 A I do know Liz, yes.</p> <p>23 Q Do you know her from professional</p> <p>24 meetings and other interactions?</p>	<p>1 Q Do you know why she's no longer an</p> <p>2 expert?</p> <p>3 A I don't.</p> <p>4 Q Do you know Dr. Huh?</p> <p>5 A I do know Dr. Huh. Warner. Uh-huh.</p> <p>6 Q Do you know why Dr. Huh is not serving</p> <p>7 as an expert for the defendants in the MDL?</p> <p>8 A No.</p> <p>9 Q Does University of Alabama know that</p> <p>10 you are serving as a paid expert for</p> <p>11 Johnson & Johnson --</p> <p>12 A Yes.</p> <p>13 Q -- in this case?</p> <p>14 Do you know how much money</p> <p>15 Johnson & Johnson has contributed to the</p> <p>16 University of Alabama and your lab?</p> <p>17 MS. CURRY:</p> <p>18 Object to the form.</p> <p>19 A I --</p> <p>20 MS. THOMPSON:</p> <p>21 Q Let me rephrase that question because I</p> <p>22 don't like being "contributed."</p> <p>23 Do you know how much money</p> <p>24 Johnson & Johnson has paid to University of</p>
Page 103	Page 105
<p>1 A I know her professionally and we're on</p> <p>2 several papers together.</p> <p>3 Q Yes, you are.</p> <p>4 A Yeah.</p> <p>5 Q Have you discussed the case with</p> <p>6 Dr. Swisher?</p> <p>7 A Not that I can recall.</p> <p>8 Q Were you aware that she was originally</p> <p>9 disclosed as an expert for the defendants?</p> <p>10 MS. CURRY:</p> <p>11 Object to the form.</p> <p>12 A I think her name did -- was sort of</p> <p>13 mentioned to me, but --</p> <p>14 MS. CURRY:</p> <p>15 And please don't reveal any discussions</p> <p>16 or --</p> <p>17 THE WITNESS:</p> <p>18 Okay.</p> <p>19 MS. CURRY:</p> <p>20 -- communications that you've had with</p> <p>21 lawyers.</p> <p>22 THE WITNESS:</p> <p>23 Yes, counsel.</p> <p>24 MS. THOMPSON:</p>	<p>1 Alabama?</p> <p>2 A No.</p> <p>3 Q Do you know how much money</p> <p>4 Johnson & Johnson has paid to support your lab?</p> <p>5 MS. CURRY:</p> <p>6 Object to the form.</p> <p>7 A None.</p> <p>8 MS. CURRY:</p> <p>9 We've been going over an hour and a</p> <p>10 half. Whenever it's a good breaking point for</p> <p>11 you.</p> <p>12 MS. THOMPSON:</p> <p>13 I think maybe less than five minutes --</p> <p>14 MS. CURRY:</p> <p>15 No problem.</p> <p>16 MS. THOMPSON:</p> <p>17 -- and it's a great break time.</p> <p>18 A I may be in kidney failure soon.</p> <p>19 MS. THOMPSON:</p> <p>20 Q Can you make five minutes?</p> <p>21 A Yeah, I can. Yeah.</p> <p>22 Q We'll -- we'll --</p> <p>23 A Sure.</p> <p>24 Q -- be in the same boat there, so we</p>

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<p style="text-align: right;">Page 106</p> <p>1 can --</p> <p>2 A Boat's not a good choice.</p> <p>3 Q Yeah. I should have used a different</p> <p>4 word there.</p> <p>5 We talked about the methodology that</p> <p>6 you applied, but -- but it's not included, per</p> <p>7 se, in the report.</p> <p>8 Can you refer to me -- me to any</p> <p>9 published article, textbook chapter, anything</p> <p>10 that actually describes Dr. Birrer's methodology?</p> <p>11 MS. CURRY:</p> <p>12 Object to the form.</p> <p>13 A No. Again, I -- I think this relates</p> <p>14 to what a lot of us in the field on my level do</p> <p>15 routinely, and so it's not really defined. But</p> <p>16 when we review literature, a topic, I wouldn't</p> <p>17 want to -- I don't want to call it a</p> <p>18 meta-analysis because that's a formal process.</p> <p>19 But we -- we -- we do the right -- we do the same</p> <p>20 thing. If we do it right, then it's</p> <p>21 comprehensive and then we make opinions on those</p> <p>22 papers. That's the methodology.</p> <p>23 MS. THOMPSON:</p> <p>24 Q Okay.</p>	<p style="text-align: right;">Page 108</p> <p>1 MS. THOMPSON:</p> <p>2 Q How about what is sometimes used in the</p> <p>3 literature, elongated mineral fibers? Does that</p> <p>4 sound familiar?</p> <p>5 A It sounds consistent with some of the</p> <p>6 things I read, but I certainly did not pursue</p> <p>7 that sort of mineralogy review.</p> <p>8 Q So no comprehensive review on what's</p> <p>9 called EMP sometimes.</p> <p>10 MS. CURRY:</p> <p>11 Object to the form.</p> <p>12 A No.</p> <p>13 MS. THOMPSON:</p> <p>14 Q And I can assume that you didn't do a</p> <p>15 comprehensive review on heavy metals --</p> <p>16 A Correct.</p> <p>17 Q -- and ovarian cancer?</p> <p>18 A Yes.</p> <p>19 Q Or fragrance chemicals and ovarian</p> <p>20 cancer?</p> <p>21 A Correct.</p> <p>22 Q Do you agree that scientists can look</p> <p>23 at the same body of literature and reach</p> <p>24 different conclusions, in a general sense?</p>
<p style="text-align: right;">Page 107</p> <p>1 A It's more of a scientific lab-based</p> <p>2 approach.</p> <p>3 Q Okay. And did you apply the same</p> <p>4 standards for this report that you would use if</p> <p>5 you were publishing a paper, for example, a</p> <p>6 review article like we discussed before?</p> <p>7 A I think so, yes.</p> <p>8 Q Would you be willing to have the</p> <p>9 opinions that you've provided in this report</p> <p>10 peer-reviewed if that were appropriate?</p> <p>11 A Essentially, yes. Yeah. Yeah.</p> <p>12 Q And I think we've discussed this, but</p> <p>13 does -- in your opinion, you performed a</p> <p>14 comprehensive literature review on the subject of</p> <p>15 talc and ovarian cancer; correct?</p> <p>16 A Correct.</p> <p>17 Q But am I correct to say that you did</p> <p>18 not perform the same comprehensive literature</p> <p>19 review for asbestos and ovarian cancer?</p> <p>20 A Correct.</p> <p>21 Q Fibrous talc in ovarian cancer?</p> <p>22 MS. CURRY:</p> <p>23 Object to the form.</p> <p>24 A Didn't use that term.</p>	<p style="text-align: right;">Page 109</p> <p>1 A You know, again, I think if the body</p> <p>2 of -- of data and literature is substantive and</p> <p>3 clear, I think that a reasonable scientist, a</p> <p>4 competent scientist will come to the same</p> <p>5 conclusion.</p> <p>6 Q So is it your opinion that a scientist</p> <p>7 who looks at the baby powder literature or talcum</p> <p>8 powder literature and concludes something</p> <p>9 different from you is unreasonable and</p> <p>10 incompetent?</p> <p>11 MS. CURRY:</p> <p>12 Object to the form.</p> <p>13 A I -- I would say they got it wrong.</p> <p>14 MS. THOMPSON:</p> <p>15 Q They got it wrong. But what about</p> <p>16 unreasonable?</p> <p>17 MS. CURRY:</p> <p>18 Object to the form.</p> <p>19 A I don't -- I wouldn't use that term. I</p> <p>20 would say that they looked at the data and</p> <p>21 misinterpreted it.</p> <p>22 MS. THOMPSON:</p> <p>23 Q And would you say the same about their</p> <p>24 competence?</p>

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<p style="text-align: right;">Page 110</p> <p>1 MS. CURRY: 2 Object to the form. 3 A I think -- you know, labeling that as 4 incompetent is not appropriate. 5 MS. THOMPSON: 6 Q Well, you said, I think that a 7 reasonable scientist, competent scientist will 8 come to the same conclusion. Wouldn't that imply 9 that if they come to a different inclusion -- 10 conclusion, that they're unreasonable or 11 incompetent? 12 A Well, I think I prefaced that with if 13 the body of science we're looking at is -- is -- 14 it's convincing and strong and reproducible, that 15 reasonable scientists will come to the same 16 conclusion. 17 When the data is really unconvincing, 18 which is what we're dealing with here -- this 19 data is not convincing -- there's no data for 20 talc being involved in ovarian cancer, then you 21 get this disparate opinions. And -- and they've 22 got it wrong. And I made the -- 23 Q They've got it -- sorry. 24 A And I've made the argument why I got it</p>	<p style="text-align: right;">Page 112</p> <p>1 A Okay. 2 MS. CURRY: 3 Can we take a break? 4 A It looks like you're coming to an end. 5 MS. THOMPSON: 6 Q We are. Well, not the end of the day. 7 The end of the section. 8 A Hope springs eternal. 9 Q Wishful thinking. 10 One -- one more question, then we're 11 done. 12 A Sure. 13 Q What does "proof" mean to you? 14 MS. CURRY: 15 Object to the form. 16 MS. THOMPSON: 17 Q In a scientific sense. 18 A That would be evidence to support the 19 conclusion. 20 Q To convincingly support the conclusion? 21 MS. CURRY: 22 Object to the form. 23 A I'm not sure I need that adjective 24 there.</p>
<p style="text-align: right;">Page 111</p> <p>1 right. 2 Q Okay. They've got it wrong? 3 A Uh-huh. 4 Q You have it right. 5 A Uh-huh. 6 Q But I'm trying to find -- figure out 7 how you think they got it wrong. Were they 8 misinformed? 9 MS. CURRY: 10 Object to the form. 11 A They misinterpreted the data. 12 MS. THOMPSON: 13 Q They misinterpreted the data. 14 A Yeah. 15 Q And you would say they misinterpreted 16 the data even though they interpreted the data in 17 the same way that the authors presenting the data 18 pre- -- interpreted it? 19 MS. CURRY: 20 Object to the form. 21 A We'd have to go through the actual 22 paper you're referring to. 23 MS. THOMPSON: 24 Q Okay. We may go through some of those.</p>	<p style="text-align: right;">Page 113</p> <p>1 MS. THOMPSON: 2 Q Well, support -- support equals proof? 3 A Support couldn't equal proof. Proof is 4 a general term. So it's gonna be a spectrum. 5 Q 100 percent? 6 A Are you -- you know, definitive proof 7 would be definitive. 8 Q Okay. Let's take a break. 9 VIDEOGRAPHER: 10 Off the record at 10:44 a.m. 11 (OFF THE RECORD.) 12 VIDEOGRAPHER: 13 We're back on the record at 11 a.m. 14 MS. THOMPSON: 15 Q Dr. Birrer, I want to give you a series 16 of statements and have you agree or disagree or, 17 if you don't know or don't have an opinion, 18 that's fine, too. And -- and if you do have a 19 comment or explanation, you're welcome to provide 20 that, too, after you -- do you have a pen? You 21 can mark on this exhibit as we go through. This 22 is Exhibit 9. 23 (DEPOSITION EXHIBIT NUMBER 9 24 WAS MARKED FOR IDENTIFICATION.)</p>

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<p style="text-align: right;">Page 114</p> <p>1 MS. CURRY: 2 Can I just state an objection on the 3 record to the creation of this exhibit without 4 knowing the background of where the statements 5 are coming from. 6 MS. GARBER: 7 I don't think we're going to have 8 speaking objections here today, Miss Curry. The 9 proper objection is "Objection. Form." Do not 10 coach the witness, please. 11 MS. CURRY: 12 Miss Garber, I'm not coaching the 13 witness. 14 MS. GARBER: 15 You are coaching the witness. You know 16 you're coaching the witness. 17 MS. THOMPSON: 18 I'm asking a statement. It doesn't 19 matter where it's coming from. It's from my 20 head. 21 MR. MIZGALA: 22 Do you have extra copies of this? 23 MS. THOMPSON: 24 I did bring extra copies.</p>	<p style="text-align: right;">Page 116</p> <p>1 A Yeah. I would disagree with that 2 statement. 3 Q Number 2, "If 40 percent of women use 4 talc and the relative risk is 1.2, then 7 percent 5 of ovarian cancer cases would be attributable to 6 talc use or 1,577 cases a year in the USA. This 7 is not a trivial number and should not be 8 dismissed." 9 Would you agree or disagree? 10 MS. CURRY: 11 Object to the form. 12 A Disagree. 13 MS. THOMPSON: 14 Q Number 3, "Genital powder use is a 15 modifiable exposure associated with small to 16 moderate increases in risk of most histologic 17 subtypes of epithelial ovarian cancer." 18 Would you agree or disagree? 19 MS. CURRY: 20 Object to the form. 21 A Disagree. 22 I'm sorry. Go ahead. Got it? 23 Disagree. 24 MS. THOMPSON:</p>
<p style="text-align: right;">Page 115</p> <p>1 MR. MIZGALA: 2 Thank you. 3 MS. THOMPSON: 4 Q So, Dr. Birrer, statement number 1, 5 "Given the number of hazard ratios reported in 6 the literature between 1.1 and" -- that should be 7 an -- "1.4 in both case-control and cohort 8 studies, it is disingenuous to state that there 9 is no evidence that talc is associated with 10 ovarian cancer." 11 Do you agree or disagree with that 12 statement? 13 MS. CURRY: 14 Object to the form. 15 A Now, you want me to write an answer 16 here? 17 MS. THOMPSON: 18 Q Yes, please. And then -- and when you 19 tell me, I'm going to put it on here, too. 20 A Yeah. Okay. In these -- the hazard 21 ratios, these are in a case-controlled cohort 22 studies. 23 Q It says in both case-controlled and 24 cohort studies.</p>	<p style="text-align: right;">Page 117</p> <p>1 Q Number 4, "Perineal use of talc-based, 2 not asbestiform, body powder is possibly 3 carcinogenic to humans, group 2B." 4 A Disagree. 5 MS. CURRY: 6 Object to the form. 7 MS. THOMPSON: 8 Q Number 5, "The use of perineal talcum 9 powder has been associated with a 20 to 30 10 percent increased risk of ovarian cancer, 11 although it also has been shown to vary by 12 histologic subtype." 13 MS. CURRY: 14 Object to the form. 15 MS. THOMPSON: 16 Q Agree or disagree? 17 A And this is -- like, histologic -- 18 clear cell and endometrioid? Is that what's 19 being implied here? 20 Q Yes. 21 A Disagree. 22 Q Number 6, "A lot of work has been done 23 to clarify the risk reduction of various 24 lifestyle approaches, such as alcohol, obesity,</p>

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<p>1 cigarette smoking and talc use. Some of these</p> <p>2 are subtype specific, such as endometriosis,</p> <p>3 cigarette smoking, while others are general risk</p> <p>4 factors. Use of talc in the genital area has</p> <p>5 consistently been shown to increase the risk of</p> <p>6 OC and therefore is not recommended."</p> <p>7 MS. CURRY:</p> <p>8 Object to the form.</p> <p>9 A Disagree.</p> <p>10 MS. THOMPSON:</p> <p>11 Q Number 7, "Inflammatory risk factors</p> <p>12 for EOC are perineal talc exposure, endometriosis</p> <p>13 and pelvic inflammatory disease."</p> <p>14 Agree or disagree?</p> <p>15 MS. CURRY:</p> <p>16 Object to the form.</p> <p>17 A So this is inclusive of all three;</p> <p>18 right? Endometriosis and --</p> <p>19 MS. THOMPSON:</p> <p>20 Q Yes.</p> <p>21 A Okay.</p> <p>22 Q But if you want to disagree and</p> <p>23 explain, that -- that's fine.</p> <p>24 A I would -- that's a tough one to</p>	<p>1 statement as a whole --</p> <p>2 A Yeah.</p> <p>3 Q -- but would --</p> <p>4 A Caveat.</p> <p>5 Q -- and that will be on the record that</p> <p>6 you --</p> <p>7 A Okay. Parsed it.</p> <p>8 Q The ones that -- yeah.</p> <p>9 Number 9, "Talc powder use is highly</p> <p>10 prevalent in the African-American community and</p> <p>11 has been found to be associated with increased</p> <p>12 risk of ovarian cancer, period."</p> <p>13 MS. CURRY:</p> <p>14 Object to the form.</p> <p>15 A So I do believe the first part, that</p> <p>16 it's prevalent in the African-American community.</p> <p>17 The second part is not convincing to me.</p> <p>18 Is that -- can we put that on the</p> <p>19 record? Disagree with the caveat, yeah.</p> <p>20 MS. THOMPSON:</p> <p>21 Q Yeah. "Most women report using</p> <p>22 Johnson's baby powder or Shower to Shower."</p> <p>23 A I don't know.</p> <p>24 Q "The average age women begin using talc</p>
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<p>1 answer. I think endometriosis is a -- I don't</p> <p>2 call it inflammatory. So, yeah, I would -- I</p> <p>3 don't call it inflammatory, so, yeah, I would</p> <p>4 disagree on this. It's too general.</p> <p>5 MS. THOMPSON:</p> <p>6 Q "Risk factors to be considered:</p> <p>7 Parity, oral contraceptive use, breastfeeding,</p> <p>8 tubal ligation, painful periods or endometriosis,</p> <p>9 obesity or polycystic ovarian syndrome, and talc</p> <p>10 use. These risk factors are concordant with</p> <p>11 published epidemiologic data related to</p> <p>12 reproductive factors, use of talc, tubal</p> <p>13 ligation, endometriosis and polycystic ovarian</p> <p>14 syndrome or obesity."</p> <p>15 MS. CURRY:</p> <p>16 Object to the form.</p> <p>17 A So parity, oral contraceptive,</p> <p>18 breastfeeding, tubal ligation, endometriosis but</p> <p>19 not painful periods or obesity or talc use. Is</p> <p>20 that a --</p> <p>21 MS. THOMPSON:</p> <p>22 Q Okay.</p> <p>23 A -- no or --</p> <p>24 Q So -- so you would disagree with the</p>	<p>1 is 20."</p> <p>2 A Don't know that.</p> <p>3 Q "In the interest of public health, I</p> <p>4 believe we should caution women against using</p> <p>5 genital talcum powder," number 12.</p> <p>6 MS. CURRY:</p> <p>7 Object to the form.</p> <p>8 MS. THOMPSON:</p> <p>9 Q Agree or disagree?</p> <p>10 A I disagree.</p> <p>11 Q Number 13, "Genital powder use is a</p> <p>12 lifestyle risk factor for all serous,</p> <p>13 endometrioid, and clear cell histologic subtypes</p> <p>14 of ovarian cancer."</p> <p>15 MS. CURRY:</p> <p>16 Object to the form.</p> <p>17 A I disagree.</p> <p>18 MS. THOMPSON:</p> <p>19 Q Number 14, "Overall, there is an</p> <p>20 association between genital talc use and EOC and</p> <p>21 a significant trend with increasing" -- in</p> <p>22 quotations -- "talc years of use."</p> <p>23 MS. CURRY:</p> <p>24 Object to the form.</p>

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<p>1 MS. THOMPSON: 2 Q Agree or disagree? 3 A I'm thinking. Disagree. 4 Q Number 15, "Talc-containing powders are 5 hypothesized to promote cancer development by 6 ascending the female genital tract and 7 interacting directly with the ovarian surface 8 epithelium, leading to local inflammation 9 characterized by increased rates of cell 10 division, DNA repair, oxidative stress, and 11 elevated inflammatory cytokines." 12 MS. CURRY: 13 Object to the form. 14 A This is a hypothesis; right? 15 MS. THOMPSON: 16 Q Yes. 17 A I agree. 18 Q "Following" -- number 16. 19 A Uh-huh. 20 Q "Following perineal application, talc 21 particles can migrate from the vagina to the 22 peritoneal cavity and ovaries." 23 MS. CURRY: 24 Object to the form.</p>	<p>1 present in the vagina, can migrate to the upper 2 genital tract." 3 MS. CURRY: 4 Object to the form. 5 MS. THOMPSON: 6 Q Agree or disagree? 7 MS. THOMPSON: 8 A You want to -- do you want to define 9 "biologic credibility"? 10 THE COURT REPORTER: 11 Say again? 12 THE WITNESS: 13 Define "biologic credibility." 14 Sorry. I'm mumbling. 15 THE COURT REPORTER: 16 Uh-huh. 17 MS. THOMPSON: 18 Q Let's define it as evidence of a 19 credible biologic mechanism. 20 A I would disagree. 21 MS. CURRY: 22 Object to the form. 23 MS. THOMPSON: 24 Q Number 20, "The vagina serves as a</p>
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<p>1 A Disagree on that. 2 MS. THOMPSON: 3 Q Number 17, "A majority of women 4 experience retrograde menstruation. This 5 suggests a mechanism by which talc particles can 6 travel through the female reproductive tract to 7 the peritoneal cavity and ovaries." 8 MS. CURRY: 9 Object to the form. 10 MS. THOMPSON: 11 Q Agree or disagree? 12 A Disagree. 13 Q Number 18, "It is possible that the 14 passage of talc is aided by retrograde menses and 15 that talc use during menses poses a special 16 risk." 17 Agree or disagree? 18 MS. CURRY: 19 Object to the form. 20 A Disagree. 21 MS. THOMPSON: 22 Q 19, "Biologic credibility of the 23 Talc/EOC association is enhanced by persuasive 24 evidence that inert particles the size of talc,</p>	<p>1 portal to the internal reproductive tract. 2 MS. CURRY: 3 Object to the form. 4 A Agree. 5 MS. THOMPSON: 6 Q 21, "The vagina is a musculoepithelial 7 tube extending from the level of the external 8 genitals to the cervical portion of the uterus. 9 It is a reproductive conduit in all respects, 10 connecting the external environment to the 11 internal genitalia." 12 MS. CURRY: 13 Object to the form. 14 A I'm not sure I understand that 15 statement. 16 What's the internal genitalia? 17 MS. THOMPSON: 18 Q The ovaries. 19 A The ovaries. I'm putting that in here. 20 Q And tubes. Let's say tubes and 21 ovaries. 22 A Okay. External. 23 Yeah, I would agree on that. 24 Q And, actually, I think the --</p>

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<p>1 A Cervix.</p> <p>2 Q I think the uterus is an internal</p> <p>3 genitalia, too.</p> <p>4 A Okay.</p> <p>5 Q But I agree that's somewhat --</p> <p>6 A Yeah. It's a little -- I mean, yeah.</p> <p>7 Genitalia is usually external.</p> <p>8 Q Yeah.</p> <p>9 22, "A review of the literature</p> <p>10 suggests that it is biologically plausible for</p> <p>11 talc particles to migrate from the vagina to the</p> <p>12 peritoneal cavity and ovaries following perineal</p> <p>13 application."</p> <p>14 MS. CURRY:</p> <p>15 Object to the form.</p> <p>16 MS. THOMPSON:</p> <p>17 Q Agree or disagree?</p> <p>18 A Disagree.</p> <p>19 Q "Talc" -- 23. "Talc placed on the</p> <p>20 perineum may enter the vagina and ascend to the</p> <p>21 upper genital tract."</p> <p>22 Agree or disagree?</p> <p>23 MS. CURRY:</p> <p>24 Object to the form.</p>	<p>1 A Disagree.</p> <p>2 MS. THOMPSON:</p> <p>3 Q 27, "Talc is able to migrate through</p> <p>4 the genital tract and gain access to the ovaries</p> <p>5 because talc fibers have been detected in benign</p> <p>6 and malignant ovarian tissues."</p> <p>7 Agree or disagree?</p> <p>8 MS. CURRY:</p> <p>9 Object to the form.</p> <p>10 A Disagree.</p> <p>11 MS. THOMPSON:</p> <p>12 Q 28, "There are inherent limitations</p> <p>13 quantifying a dose-response due to a lack of</p> <p>14 metrics for how much talc is in an application,</p> <p>15 how much enters the vagina, and how much reaches</p> <p>16 the upper genital tract where, presumably, any</p> <p>17 deleterious effect is mediated. This may account</p> <p>18 for the failure to identify a dose-response in</p> <p>19 many papers on talc and ovarian cancer."</p> <p>20 MS. CURRY:</p> <p>21 Object to the form.</p> <p>22 A It's a big statement. Give me a</p> <p>23 second. I disagree with that.</p> <p>24 MS. THOMPSON:</p>
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<p>1 A Disagree.</p> <p>2 MS. THOMPSON:</p> <p>3 Q 24, "The potential for particulates to</p> <p>4 migrate from the perineum and vagina to the</p> <p>5 peritoneal cavity is indisputable."</p> <p>6 MS. CURRY:</p> <p>7 Object to the form.</p> <p>8 A Disagree.</p> <p>9 MS. THOMPSON:</p> <p>10 Q "The Sjösten study" --</p> <p>11 Do you know the Sjösten study?</p> <p>12 A I do.</p> <p>13 Q -- "offers compelling evidence in</p> <p>14 support of the migration hypothesis."</p> <p>15 MS. CURRY:</p> <p>16 Object to the form.</p> <p>17 A Disagree.</p> <p>18 MS. THOMPSON:</p> <p>19 Q 26, "Talc particulates from perineal</p> <p>20 application have been shown to migrate to the</p> <p>21 ovaries."</p> <p>22 Agree or disagree?</p> <p>23 MS. CURRY:</p> <p>24 Object to the form.</p>	<p>1 Q 29, "Tubal ligation is a strong</p> <p>2 protective factor. One possibility for the</p> <p>3 mechanism is blocking the transience of potential</p> <p>4 materials that could impact the health of the</p> <p>5 fimbria."</p> <p>6 MS. CURRY:</p> <p>7 Object to the form.</p> <p>8 A Disagree.</p> <p>9 MS. THOMPSON:</p> <p>10 Q Number 30, "Any material -- whether it</p> <p>11 be talc, heavy metals, asbestos, whatever -- can</p> <p>12 migrate from the perineum to the ovaries through</p> <p>13 the reproductive tract. There's an anatomical</p> <p>14 conduit, so it's not blocked. Theoretically, it</p> <p>15 could happen."</p> <p>16 Agree or disagree?</p> <p>17 MS. CURRY:</p> <p>18 Object to the form.</p> <p>19 A Disagree.</p> <p>20 MS. THOMPSON:</p> <p>21 Q 31, "There is an anatomic conduit from</p> <p>22 the perineum through to the ovary, vagina,</p> <p>23 cervical os, endometrium, and the fallopian tube</p> <p>24 that is, in most women, an open conduit -- that</p>

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<p style="text-align: right;">Page 130</p> <p>1 is in most women an open conduit. On a theoretic 2 level, things can transit." 3 A I would agree with that. 4 MS. CURRY: 5 Object to the form. Sorry. 6 THE WITNESS: 7 I'm sorry. 8 MS. THOMPSON: 9 Q 32, "Genital powder use was associated 10 with ovarian cancer risk in African-American 11 women and are consistent with localized chronic 12 inflammation in the ovary due to particulates 13 that travel through a direct transvaginal route." 14 MS. CURRY: 15 Object to the form. 16 A Disagree. 17 MS. THOMPSON: 18 Q 33, "Biologic credibility for an 19 association would be strengthened by an animal 20 model, but an experiment capturing all of the 21 potential factors in the 'human' model would be 22 very difficult. These elements include 23 chronicity of the exposure, anatomic and 24 physiologic uniqueness of women, effects of</p>	<p style="text-align: right;">Page 132</p> <p>1 Oh, sorry. 2 So the animal model, yes. The rest of 3 it, no. 4 Q Animal model -- 5 A Would be strengthened. 6 Q Okay. We've got in the human model -- 7 A Yeah. 8 Q -- agree. 9 A Okay. 10 Q Okay. And the rest, disagree. 11 A Yeah. 12 Q Okay. I think that's clear, especially 13 with explanation. 14 34, "It is plausible that perineal 15 talc, and other particulate, in parens, that 16 reaches the endometrial cavity, fallopian tubes, 17 ovaries and peritoneum, may elicit a foreign 18 body-type reaction and inflammatory response 19 that, in some exposed women, may progress to 20 epithelial cancers." 21 MS. CURRY: 22 Object to the form. 23 A I disagree with that. 24 MS. THOMPSON:</p>
<p style="text-align: right;">Page 131</p> <p>1 pregnancy and potential spread through coitus." 2 Agree or disagree? 3 MS. CURRY: 4 Object to the form. 5 A This is in relationship to talc? 6 MS. THOMPSON: 7 Q Yes. 8 A Okay. 9 Q Talc and ovarian cancer. 10 A Yeah, yeah. Okay. 11 It's a two-part issue, unfortunately. 12 I mean, I think it would be strengthened by an 13 animal model. 14 Q And if you -- if you'd -- if you'd like 15 to divide that up into two sections, that would 16 be -- that's fine. 17 A Okay. Well, I -- okay. That's -- 18 yeah. I think -- I think it would be 19 strengthened by an animal model. 20 Q Okay. So -- 21 A "Experiment capturing all the potential 22 would be difficult." 23 I don't agree with that, the second 24 part. Can I do that and split it a little bit?</p>	<p style="text-align: right;">Page 133</p> <p>1 Q 35, "Epidemiologic evidence implicates 2 chronic inflammation as a central mechanism in 3 the pathogenesis of ovarian cancer, the most 4 lethal gynecologic cancer among women in the 5 United States." 6 MS. CURRY: 7 Object to the form. 8 MS. THOMPSON: 9 Q And I'll assume that you don't agree 10 with the last -- 11 A Right. Most lethal? 12 Q -- part of that? But the first part? 13 A I would disagree with this. Yeah. 14 Q 36, "Findings on talc and endometriosis 15 are consistent with previous findings and are 16 compatible with a hypothesis that these factors 17 increase the risk of ovarian cancer and that 18 inflammation -- and that inflammation may be a 19 common pathway." 20 MS. CURRY: 21 Object to the form. 22 A Disagree. 23 MS. THOMPSON: 24 Q 37, "Chron-" --</p>

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<p style="text-align: right;">Page 134</p> <p>1 A 37. Right.</p> <p>2 Q "Chronic inflammation has been proposed</p> <p>3 as the possible causal mechanism that explains</p> <p>4 the observed association between certain risk</p> <p>5 factors, such as use of talcum powder (talc) in</p> <p>6 the pelvic region and epithelial ovarian cancer."</p> <p>7 MS. CURRY:</p> <p>8 Object to the form.</p> <p>9 A That's been proposed; right? I would</p> <p>10 agree.</p> <p>11 MS. THOMPSON:</p> <p>12 Q And you would disagree that that is a</p> <p>13 possible cause of mechanism, I assume.</p> <p>14 A Correct.</p> <p>15 Q 38, "Talc particles can induce an</p> <p>16 inflammatory response in vivo, which may be</p> <p>17 important in ovarian cancer risk. Normal ovarian</p> <p>18 cells treated with talc are more likely to</p> <p>19 undergo cell proliferation and neoplastic</p> <p>20 transformation, and cellular generation of</p> <p>21 reactive oxygen species increases with increasing</p> <p>22 exposure to talc."</p> <p>23 MS. CURRY:</p> <p>24 Object to the form.</p>	<p style="text-align: right;">Page 136</p> <p>1 inflammation and an increased risk of ovarian</p> <p>2 cancer. Other specific inflammatory factors have</p> <p>3 also been associated with ovarian cancer."</p> <p>4 MS. CURRY:</p> <p>5 Object to the form.</p> <p>6 A I agree on that.</p> <p>7 MS. THOMPSON:</p> <p>8 Q 42, "The patency of the female tract</p> <p>9 and the nature of ovarian cancer as a surface</p> <p>10 epithelial (mesothelial lesion) make the ovary a</p> <p>11 target for foreign body carcinogenesis."</p> <p>12 MS. CURRY:</p> <p>13 Object to the form.</p> <p>14 MS. THOMPSON:</p> <p>15 Q Agree or disagree?</p> <p>16 A Disagree.</p> <p>17 Q 43, "Inflammation has been suggested to</p> <p>18 be a major factor leading to epithelial ovarian</p> <p>19 cancer. For example, epidemiologic data have</p> <p>20 shown that asbestos and talc exposure increased</p> <p>21 ovarian cancer risk."</p> <p>22 MS. CURRY:</p> <p>23 Object to the form.</p> <p>24 A Disagree.</p>
<p style="text-align: right;">Page 135</p> <p>1 A I disagree with that.</p> <p>2 MS. THOMPSON:</p> <p>3 Q 39, "A growing body of epidemiologic</p> <p>4 evidence suggests that factors causing epithelial</p> <p>5 inflammation are involved in ovarian</p> <p>6 carcinogenesis. Such factors include asbestos</p> <p>7 and talc exposures, endometriosis and pelvic</p> <p>8 inflammatory disease (PID)."</p> <p>9 MS. CURRY:</p> <p>10 Object to the form.</p> <p>11 A Disagree with that.</p> <p>12 MS. THOMPSON:</p> <p>13 Q 40, "Direct induction of inflammation</p> <p>14 as a result of endometriosis, talc, and asbestos</p> <p>15 exposure, and PID, as well as ovulation itself,</p> <p>16 may act to promote ovarian tumorigenesis."</p> <p>17 Agree or disagree?</p> <p>18 MS. CURRY:</p> <p>19 Object to the form.</p> <p>20 A Disagree.</p> <p>21 MS. THOMPSON:</p> <p>22 Q 41, regarding Inflammation. "Studies</p> <p>23 of the inflammatory marker C-reactive protein</p> <p>24 suggests a possible association between</p>	<p style="text-align: right;">Page 137</p> <p>1 MS. THOMPSON:</p> <p>2 Q 44, "Studies have found" -- "also found</p> <p>3 that endometrio-" --</p> <p>4 Let's leave out the "also," since I</p> <p>5 don't know what that refers to.</p> <p>6 "Studies have found that endometriosis,</p> <p>7 pelvic inflammatory disease, and mumps viral</p> <p>8 infection are positively associated with ovarian</p> <p>9 cancer risk. In contrast, tubal ligations and</p> <p>10 hysterectomies, which are thought to reduce the</p> <p>11 exposure of the OSE to environmental inflammation</p> <p>12 initiators have been shown to reduce the risk of</p> <p>13 ovarian cancer."</p> <p>14 MS. CURRY:</p> <p>15 Object to the form.</p> <p>16 A I agree on that.</p> <p>17 MS. THOMPSON:</p> <p>18 Q 45, "It has been noted that the</p> <p>19 ovulatory process itself resembles an</p> <p>20 inflammatory reaction, with leukocytic</p> <p>21 infiltration, the release of nitric oxide and</p> <p>22 inflammatory cytokines, basal dilation, DNA</p> <p>23 repair and tissue remodeling."</p> <p>24 MS. CURRY:</p>

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<p>1 Object to the form.</p> <p>2 MS THOMPSON:</p> <p>3 Q Agree or disagree?</p> <p>4 A I would agree on that.</p> <p>5 Q 46, "The latency period of more</p> <p>6 advanced, malignant epithelial ovarian cancer</p> <p>7 could be estimated to be approximately 30 to 40</p> <p>8 years."</p> <p>9 MS. CURRY:</p> <p>10 Form.</p> <p>11 A I don't know that. Sorry. I don't</p> <p>12 know.</p> <p>13 MS. THOMPSON:</p> <p>14 Q "If the magnitude of the association is</p> <p>15 to be estimated with precision, it is important</p> <p>16 that consortia are developed and expanded in</p> <p>17 order to generate the appropriate sample size."</p> <p>18 And this is in regard to talcum powder</p> <p>19 in association with ovarian cancer.</p> <p>20 MS. CURRY:</p> <p>21 Object to the form.</p> <p>22 A Don't know.</p> <p>23 MS. THOMPSON:</p> <p>24 Q 48, "Neither prospective study" --</p>	<p>1 Q 51, "For baby powder users, it is habit</p> <p>2 that developed at one point and stays regularly."</p> <p>3 MS. CURRY:</p> <p>4 Object to the form.</p> <p>5 A Don't know.</p> <p>6 MS. THOMPSON:</p> <p>7 Q 52, "In order to achieve statistical</p> <p>8 significance in a prospective study, we need a</p> <p>9 much larger cohort. For example, we will need to</p> <p>10 study upwards of 200,000 women for ten years."</p> <p>11 MS. CURRY:</p> <p>12 Object to the form.</p> <p>13 A I disagree.</p> <p>14 MS. THOMPSON:</p> <p>15 Q You disagree.</p> <p>16 53, "Given inherent limitation of</p> <p>17 cohort studies, it is not surprising that we have</p> <p>18 not been able to confirm the case-control studies</p> <p>19 with prospective studies, but this does not mean</p> <p>20 that the case-control studies were wrong."</p> <p>21 MS. CURRY:</p> <p>22 Object to the form.</p> <p>23 A Disagree.</p> <p>24 MS. THOMPSON:</p>
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<p>1 meaning Gertig or Houghton -- "confirmed the</p> <p>2 association of talc use and ovarian cancer raised</p> <p>3 by the case-control studies, but neither study</p> <p>4 was powered to detect a risk of 1.2 and</p> <p>5 therefore, we cannot exclude the possibility."</p> <p>6 Agree or disagree?</p> <p>7 MS. CURRY:</p> <p>8 Object to the form.</p> <p>9 A Disagree.</p> <p>10 MS. THOMPSON:</p> <p>11 Q 49, "An odds ratio of 1.2 or 1.3 has no</p> <p>12 meaningful clinical impact on a patient."</p> <p>13 MS. CURRY:</p> <p>14 Object to the form.</p> <p>15 A Don't know.</p> <p>16 MS. THOMPSON:</p> <p>17 Q "There are design studies with" --</p> <p>18 sorry.</p> <p>19 50, "There are design issues with every</p> <p>20 study, both case-controls and cohort studies."</p> <p>21 MS. CURRY:</p> <p>22 Object to the form.</p> <p>23 A I would agree with that.</p> <p>24 MS. THOMPSON:</p>	<p>1 Q Agree or disagree?</p> <p>2 A Disagree.</p> <p>3 Q 54, "It is unlikely that the</p> <p>4 association between talc and ovarian cancer is</p> <p>5 due to confounding, and so it is fair to say that</p> <p>6 if there is a statistically robust relationship</p> <p>7 between talc use and ovarian cancer" -- sorry.</p> <p>8 I'm gonna start all over.</p> <p>9 "It is unlikely that the association</p> <p>10 between talc and ovarian cancer is due to</p> <p>11 confounding, and so it is fair to say that if</p> <p>12 there is a statistically robust relationship</p> <p>13 between talc use and ovarian cancer, it is likely</p> <p>14 to be causal (albeit with intermediate factors</p> <p>15 such as inflammation)."</p> <p>16 Agree or disagree?</p> <p>17 MS. CURRY:</p> <p>18 Object to the form.</p> <p>19 A Disagree.</p> <p>20 MS. THOMPSON:</p> <p>21 Q 55, "Among many epidemiologic</p> <p>22 variables, no confounders for the association --</p> <p>23 for the association were identified."</p> <p>24 MS. CURRY:</p>

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<p>1 Object to the form.</p> <p>2 A No opinion.</p> <p>3 MS. THOMPSON:</p> <p>4 Q 56, "There is a consistent association</p> <p>5 between talc and ovarian cancer that appears</p> <p>6 unlikely to be explained by recall or</p> <p>7 confounding."</p> <p>8 Agree or disagree?</p> <p>9 MS. CURRY:</p> <p>10 Object to the form.</p> <p>11 A Disagree.</p> <p>12 MS. THOMPSON:</p> <p>13 Q 57, "The meta-analyses of the available</p> <p>14 human studies in the peer-reviewed literature</p> <p>15 indicate a consistent and statistically</p> <p>16 significant positive association between perineal</p> <p>17 exposure to talc and ovarian cancer."</p> <p>18 MS. CURRY:</p> <p>19 Object to the form.</p> <p>20 A Disagree.</p> <p>21 MS. THOMPSON:</p> <p>22 Q You disagree.</p> <p>23 58, "In studies where the exposure is</p> <p>24 simple (e.g., never versus ever use), recall bias</p>	<p>1 Object to the form.</p> <p>2 A I agree on that.</p> <p>3 MS. THOMPSON:</p> <p>4 Q 61, "The gold standard for translating</p> <p>5 epidemiologic case-controlled or cohort</p> <p>6 observational studies into a clinical meaningful</p> <p>7 data relies on laboratory-derived experiments in</p> <p>8 vitro or in vivo."</p> <p>9 MS. CURRY:</p> <p>10 Object to the form.</p> <p>11 A I disagree with that.</p> <p>12 MS. THOMPSON:</p> <p>13 Q On what basis?</p> <p>14 A The -- it depends upon the</p> <p>15 epidemiologic date that that we're talking about.</p> <p>16 Q In other words, if the epidemiologic</p> <p>17 data isn't strong enough, in your opinion, then</p> <p>18 doing in vitro or in vivo studies don't provide</p> <p>19 clinically meaningful data? Is that --</p> <p>20 MS. CURRY:</p> <p>21 Object to the form.</p> <p>22 A It's actually -- it's actually the</p> <p>23 other way around. So I think if it's a weak</p> <p>24 association, then the laboratory data becomes</p>
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<p>1 is unlikely to be an important source of bias."</p> <p>2 Agree or disagree?</p> <p>3 MS. CURRY:</p> <p>4 Object to the form.</p> <p>5 A No opinion.</p> <p>6 MS. THOMPSON:</p> <p>7 Q Is that an issue that you would be</p> <p>8 inclined to -- to ask an epidemiologist?</p> <p>9 MS. CURRY:</p> <p>10 Object to the form.</p> <p>11 A I'd like to see the -- I'd like to see</p> <p>12 the study that it's based on.</p> <p>13 MS. THOMPSON:</p> <p>14 Q Okay. 59, "Available data are</p> <p>15 indicative of a causal effect." And again,</p> <p>16 referring to talc and ovarian cancer.</p> <p>17 MS. CURRY:</p> <p>18 Object to the form.</p> <p>19 A Disagree.</p> <p>20 MS. THOMPSON:</p> <p>21 Q 60, "The data supporting the</p> <p>22 association of talc to the development of ovarian</p> <p>23 cancer is completely inconclusive."</p> <p>24 MS. CURRY:</p>	<p>1 that much more important for biologic</p> <p>2 plausibility.</p> <p>3 If it has -- you know, if it's chimney</p> <p>4 sweeps or lung cancer with smoking, then that's</p> <p>5 clinically meaningful. Those effects are huge.</p> <p>6 That's what I'm -- I'm not associating this just</p> <p>7 with the talc statement. Is it a talc statement?</p> <p>8 MS. THOMPSON:</p> <p>9 Q Uh-huh. I just want to make -- just</p> <p>10 want to make sure that I understand the -- the</p> <p>11 reason for your disagreement. But if you feel</p> <p>12 like it's explained, I'm good.</p> <p>13 A And again, I -- it's sort of the broad</p> <p>14 view that if -- if the -- if the epidemiologic</p> <p>15 case control and cohort studies are so powerful</p> <p>16 with a huge effect, then the biologic experiments</p> <p>17 and lab become less important.</p> <p>18 The other way around, which is really</p> <p>19 what we're dealing with with talc where the</p> <p>20 epidemiologic data I think is not compelling, the</p> <p>21 biologic plausibility becomes more important.</p> <p>22 And it sort of gets back into the Bradford Hill.</p> <p>23 Q Okay. So it's sort of inversely</p> <p>24 proportional in terms of the --</p>

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<p>1 A In terms of value.</p> <p>2 Q -- the importance of it?</p> <p>3 A Yeah.</p> <p>4 Q Okay. Got it.</p> <p>5 62, "Mineral talc occurs naturally in a</p> <p>6 platy, flat form, but may also occur as</p> <p>7 asbestiform fibers, which describes its physical</p> <p>8 form and does not imply the presence of asbestos.</p> <p>9 The purer forms, approximately 90 percent mineral</p> <p>10 talc, are used for" -- oops -- "are used for</p> <p>11 cosmetic and hygiene products, including baby</p> <p>12 powders and feminine hygiene products."</p> <p>13 MS. CURRY:</p> <p>14 Object to the form.</p> <p>15 MS. THOMPSON:</p> <p>16 Q Agree or disagree or no opinion?</p> <p>17 A No opinion.</p> <p>18 Q That's it. I'll think of some new</p> <p>19 questions.</p> <p>20 A I feel like I just took my boards.</p> <p>21 Q Dr. Birrer, how do you define a</p> <p>22 carcinogen?</p> <p>23 A That's an agent or substance which</p> <p>24 causes or induces cancer.</p>	<p>1 Q Are you familiar with the term -- and I</p> <p>2 believe this is more in the toxicological</p> <p>3 literature -- of a complete carcinogen?</p> <p>4 A I would --</p> <p>5 Q Does that have a meaning to you?</p> <p>6 A Yeah. I've seen that described.</p> <p>7 Frankly, I can only -- I can only sort of guess</p> <p>8 what they mean by that. My guess is a complete</p> <p>9 carcinogen, putting out there for the discussion</p> <p>10 between you and me is what I'm describing as the</p> <p>11 classic initiation molecule.</p> <p>12 Q IARC describes -- do I have it? Would</p> <p>13 you look at Exhibit 6, which is the IARC? I just</p> <p>14 wanted to look at their definition of</p> <p>15 carcinogenesis and see whether you would agree</p> <p>16 with it or not.</p> <p>17 A Is it in the preamble?</p> <p>18 Q It's in the preamble. And if I can't</p> <p>19 find it, we may come back to that later.</p> <p>20 Because I can't remember where it is.</p> <p>21 Let's come back to that.</p> <p>22 A It's a big preamble.</p> <p>23 Q Lots of methodology.</p> <p>24 Are you familiar with the Hanahan paper</p>
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<p>1 Q Do you include effect on the promotion</p> <p>2 and progression of cancer as well in a -- when</p> <p>3 you're considering carcinogenicity?</p> <p>4 MS. CURRY:</p> <p>5 Object to the form.</p> <p>6 A So historically -- and there's been a</p> <p>7 lot of work on this for decades -- carcinogens</p> <p>8 have been -- usually been associated with</p> <p>9 initiation. So this is a substance -- just to</p> <p>10 you an example. Paint it on to a mouse skin, and</p> <p>11 you develop tumors above -- statistically</p> <p>12 significantly above background.</p> <p>13 Tumor promoters don't do that. But</p> <p>14 when you combine the tumor promoter with the</p> <p>15 carcinogen, instead of getting the 10 tumors, now</p> <p>16 you get a hundred. So promotion is a little bit</p> <p>17 different. That's the historic perspective.</p> <p>18 You know, we've come a long way since</p> <p>19 then, and I think it's gotten even more complex,</p> <p>20 that there are tumor promoters that work by</p> <p>21 transcriptional factors. So that's not genetic</p> <p>22 changes in the tumor, in the cells. Carcinogens</p> <p>23 usually work that way, where you're getting a</p> <p>24 permanent genetic change.</p>	<p>1 from 2011 "Hallmarks of Cancer"?</p> <p>2 A It's a global sort of review. Yes.</p> <p>3 Q A big review --</p> <p>4 A Big.</p> <p>5 Q -- article?</p> <p>6 A Is it --</p> <p>7 Q Do you know -- do you know Dr. Hanahan</p> <p>8 or know of Dr. Hanahan?</p> <p>9 A I know of him.</p> <p>10 Q And it's Hanahan and Weinberg?</p> <p>11 A Weinberg, yeah. Yeah.</p> <p>12 Q Let me go ahead and mark that.</p> <p>13 A Okay.</p> <p>14 (DEPOSITION EXHIBIT NUMBER 10</p> <p>15 WAS MARKED FOR IDENTIFICATION.)</p> <p>16 MS. THOMPSON:</p> <p>17 Make sure those don't have my markings</p> <p>18 on it.</p> <p>19 A It would be easier for me if the</p> <p>20 markings were there.</p> <p>21 MS. THOMPSON:</p> <p>22 Q Exhibit 10. And you agree that this</p> <p>23 article describes the hallmarks of cancer in a</p> <p>24 general sense; right?</p>

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<p style="text-align: right;">Page 150</p> <p>1 A Correct.</p> <p>2 Q And it's a review article in Cell. Are</p> <p>3 you familiar with that journal?</p> <p>4 A I am.</p> <p>5 Q Have you published in that journal?</p> <p>6 Probably.</p> <p>7 A I wished I had published more in that</p> <p>8 journal. Yeah.</p> <p>9 Q And it's -- the title of the article is</p> <p>10 "The Hallmarks of Cancer: The Next Generation."</p> <p>11 But in the top right hand, it says, "Leading edge</p> <p>12 review." So that would be a review article for a</p> <p>13 general audience. Would you agree?</p> <p>14 A Yes. General audience of scientists,</p> <p>15 yeah. Because it's pretty sophisticated.</p> <p>16 Q Agree.</p> <p>17 And it describes the hallmarks of</p> <p>18 cancer generally. These do not specifically</p> <p>19 apply to ovarian cancer in -- in the</p> <p>20 introduction. I'm starting on the third</p> <p>21 sentence. "They include sustaining proliferative</p> <p>22 signaling, evading growth suppressors, resisting</p> <p>23 cell death, enabling replicative" --</p> <p>24 A Third line of -- you're in the abstract</p>	<p style="text-align: right;">Page 152</p> <p>1 Characteristics."</p> <p>2 And it says, the first sentence, "An</p> <p>3 increasing body of research suggests that two</p> <p>4 additional hallmarks of cancer are involved in</p> <p>5 the pathogenesis of some and perhaps all</p> <p>6 cancers."</p> <p>7 I'm gonna skip down to the -- to the</p> <p>8 last sentence in that description.</p> <p>9 "Inflammation" --</p> <p>10 A You're in the figure legend?</p> <p>11 Q In the figure legend.</p> <p>12 "Inflammation by innate immune cells</p> <p>13 designed to fight infections and heal wounds can</p> <p>14 instead result in their inadvertent support of</p> <p>15 multiple hallmark capabilities, thereby</p> <p>16 manifesting the now widely appreciated tumor</p> <p>17 promoting consequences of inflammatory</p> <p>18 responses."</p> <p>19 Would you agree with that statement, in</p> <p>20 a general sense?</p> <p>21 A Yes.</p> <p>22 MS. CURRY:</p> <p>23 Object to the form.</p> <p>24 A Sorry.</p>
<p style="text-align: right;">Page 151</p> <p>1 or in the introduction?</p> <p>2 Q I'm in the -- sorry. I'm in the</p> <p>3 abstract.</p> <p>4 A Okay.</p> <p>5 Q It sort of seemed more like an</p> <p>6 introduction than an abstract to me. So starting</p> <p>7 again. Talking about the hallmarks described in</p> <p>8 this paper, "They include sustaining</p> <p>9 proliferative signalling, evading growth</p> <p>10 suppressors, resisting cell death, enabling</p> <p>11 replicative immortality, enduing angiogenesis,</p> <p>12 and activating invasion and metastasis.</p> <p>13 "Underlining these hallmarks are genome</p> <p>14 instability which generates the genetic diversity</p> <p>15 that expedites their acquisition and</p> <p>16 inflammation, which fosters multiple hallmark</p> <p>17 functions."</p> <p>18 Would you agree with that statement</p> <p>19 from this article?</p> <p>20 A I think as a general statement, yes.</p> <p>21 Q And the article, as you described, is</p> <p>22 quite technical and -- and goes on for a while.</p> <p>23 I'm looking at the Figure 3 on page 658. And the</p> <p>24 heading is "Emerging Hallmarks and Enabling</p>	<p style="text-align: right;">Page 153</p> <p>1 MS. THOMPSON:</p> <p>2 Q Are you familiar with Dr. Balkwill?</p> <p>3 A We're done with this?</p> <p>4 Q We're done with that.</p> <p>5 A Fran? Fran Balkwill? Yes.</p> <p>6 Q And I believe you published with</p> <p>7 Dr. Balkwill?</p> <p>8 A I believe we're on two. I can't</p> <p>9 remember.</p> <p>10 Q And she is a well-renowned cancer</p> <p>11 biologist. Would you agree?</p> <p>12 A I would agree.</p> <p>13 MS. CURRY:</p> <p>14 Object to the form.</p> <p>15 (DEPOSITION EXHIBIT NUMBER 11</p> <p>16 WAS MARKED FOR IDENTIFICATION.)</p> <p>17 MS. THOMPSON:</p> <p>18 Q I'm gonna mark as Exhibit 11 an article</p> <p>19 written by Dr. Balkwill.</p> <p>20 Have you seen this article, Dr. Birrer?</p> <p>21 A I'm actually not familiar with this.</p> <p>22 But I know Fran's work pretty well.</p> <p>23 Q Okay. Well, let's just --</p> <p>24 A Yeah.</p>

39 (Pages 150 to 153)

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<p>1 Q -- look through it. And this is also a</p> <p>2 review article.</p> <p>3 A Uh-huh.</p> <p>4 Q And -- and this article is in -- is in</p> <p>5 The Lancet. Correct?</p> <p>6 A Correct.</p> <p>7 Q And is -- we've already mentioned that</p> <p>8 Dr. Balkwill is well regarded.</p> <p>9 Is The Lancet a well-regarded journal?</p> <p>10 A Yes.</p> <p>11 MS. CURRY:</p> <p>12 Object to the form.</p> <p>13 MS. THOMPSON:</p> <p>14 Q Is it one of the most respected</p> <p>15 journals, would you say?</p> <p>16 MS. CURRY:</p> <p>17 Object to the form.</p> <p>18 A It's not as good as Cell.</p> <p>19 MS. THOMPSON:</p> <p>20 Q Oh. I won't tell them you said that.</p> <p>21 But, generally -- generally speaking --</p> <p>22 A Yes.</p> <p>23 Q -- physicians and scientists would</p> <p>24 recognize The Lancet?</p>	<p>1 progression, and immunosuppression than they are</p> <p>2 to mount an effective host antitumor response.</p> <p>3 Moreover cancer suscep- -- susceptibility and</p> <p>4 severity may be associated with functional</p> <p>5 polymorphisms of inflammatory cytokine genes, and</p> <p>6 deletion or inhibition of inflammatory cytokines,</p> <p>7 inhibits development of experimental cancer.</p> <p>8 "If genetic damage is the 'match that</p> <p>9 lights the fire' of cancer, some types of</p> <p>10 inflammation may provide the 'fuel that feeds the</p> <p>11 flames.'"</p> <p>12 That was a long passage, but do you</p> <p>13 generally agree with the statement by</p> <p>14 Dr. Balkwill?</p> <p>15 MS. CURRY:</p> <p>16 Object to the form.</p> <p>17 A I do.</p> <p>18 MS. THOMPSON:</p> <p>19 Q And then look down on that same page to</p> <p>20 panel 1.</p> <p>21 A Uh-huh.</p> <p>22 Q And the title of that panel, for lack</p> <p>23 of better word, is "Some Associations Between</p> <p>24 Inflammation and Cancer Risk." Right?</p>
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<p>1 A It's well read -- it's well read and</p> <p>2 it's -- it has a substantial impact factor.</p> <p>3 Q And we don't know in this situation</p> <p>4 whether Dr. Balkwill -- do you know</p> <p>5 Dr. Mantovani, the second author on this paper?</p> <p>6 A No. I don't recognize him.</p> <p>7 Q We don't know whether this article was</p> <p>8 invited or submitted, but, regardless, certainly</p> <p>9 the readers of Lancet would look to Dr. Balkwill</p> <p>10 as being an expert to discuss inflammation in</p> <p>11 cancer; correct?</p> <p>12 MS. CURRY:</p> <p>13 Object to the form.</p> <p>14 A Correct.</p> <p>15 MS. THOMPSON:</p> <p>16 Q So reading in -- in the abstract, which</p> <p>17 looks like an introduction to me again, but</p> <p>18 reading the abstract, "This article reviews" --</p> <p>19 second line -- "This article reviews the links</p> <p>20 between cancer and inflammation and discusses the</p> <p>21 implications of these links for cancer prevention</p> <p>22 and treatment. We suggest that the inflammatory</p> <p>23 cells and cytokines found in tumors are more</p> <p>24 likely to contribute to tumor growth,</p>	<p>1 A 901. Got it.</p> <p>2 Q And under "Malignancy," it lists</p> <p>3 various types of cancer in which there's</p> <p>4 association between inflammation and cancer risk.</p> <p>5 Correct?</p> <p>6 A Correct.</p> <p>7 Q And one of them -- one of them is</p> <p>8 ovarian; right?</p> <p>9 A I see it.</p> <p>10 Q And in the -- under the inflammatory</p> <p>11 stimulus/condition, it lists pelvic inflammatory</p> <p>12 disease, talc, tissue remodeling.</p> <p>13 Do you agree that Dr. Balkwill, at</p> <p>14 least in 2001, believed that talc was an</p> <p>15 inflammatory stimulus and condition for the</p> <p>16 association with ovarian cancer?</p> <p>17 MS. CURRY:</p> <p>18 Object to the form.</p> <p>19 A Yeah. So, again, this is a -- a bit of</p> <p>20 a recurring theme in the sense that I don't know</p> <p>21 if Fran -- I haven't talked to her about this</p> <p>22 review. I don't know if Fran believed that and</p> <p>23 got it wrong or, more likely, this is a review</p> <p>24 article. So you include everything, even though</p>

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<p style="text-align: right;">Page 158</p> <p>1 she may not feel really strongly about that. So</p> <p>2 it's a little hard to tell.</p> <p>3 MS. THOMPSON:</p> <p>4 Q But you would agree that both -- both</p> <p>5 Dr. Balkwill and The Lancet would not include</p> <p>6 something in a review article for which there was</p> <p>7 no evidence?</p> <p>8 MS. CURRY:</p> <p>9 Object to the form.</p> <p>10 A Again, it depends on how they're</p> <p>11 proposing it; that there has been -- there has --</p> <p>12 there have been reports associating PID, talc --</p> <p>13 I don't know what tissue remodeling is, although</p> <p>14 that is probably the most reasonable -- but PID</p> <p>15 and talc as associated with a risk for ovarian</p> <p>16 cancer. That's a true statement. I don't -- and</p> <p>17 the reason we're here today is because I reviewed</p> <p>18 that literature and I don't believe the</p> <p>19 conclusion.</p> <p>20 But you could put it into review.</p> <p>21 That's -- that's the nature of a review article.</p> <p>22 We all put things in that we feel the reader</p> <p>23 needs to see to get a full understanding of</p> <p>24 science, but we don't necessarily -- we're not</p>	<p style="text-align: right;">Page 160</p> <p>1 them to say, okay, this has been studied</p> <p>2 epidemiologically and in other situations. So I</p> <p>3 think -- I think that's what you're grappling</p> <p>4 with. It's a review article. So these things</p> <p>5 show up.</p> <p>6 Q Okay. So -- so there are two</p> <p>7 possibilities --</p> <p>8 A Uh-huh.</p> <p>9 Q -- it sounds like. Either Dr. Balkwill</p> <p>10 got it wrong --</p> <p>11 A Uh-huh.</p> <p>12 Q -- or because this was a review</p> <p>13 article, she was reporting evidence that was in</p> <p>14 the literature that she felt that readers of this</p> <p>15 article should be aware of.</p> <p>16 A Correct. Don't tell her I said the</p> <p>17 former.</p> <p>18 MS. CURRY:</p> <p>19 Object to the form of the question.</p> <p>20 MS. THOMPSON:</p> <p>21 Q Okay. I -- I -- I will do that for</p> <p>22 you, Dr. Birrer.</p> <p>23 A Uh-huh.</p> <p>24 Q And -- and this paper is not recent,</p>
<p style="text-align: right;">Page 159</p> <p>1 convinced.</p> <p>2 MS. THOMPSON:</p> <p>3 Q Well, but -- but back to my question,</p> <p>4 which I think was Dr. Balkwill and The Lancet</p> <p>5 would not have put this in with no evidence.</p> <p>6 MS. CURRY:</p> <p>7 Object to the form.</p> <p>8 A I don't agree with that.</p> <p>9 MS. THOMPSON:</p> <p>10 Q You think they would put something in</p> <p>11 that they did not believe there was any evidence</p> <p>12 to support?</p> <p>13 MS. CURRY:</p> <p>14 Object to the form.</p> <p>15 A Again, it depends on how you define</p> <p>16 that. So when you say "no evidence," you mean no</p> <p>17 epidemiologic studies that have ever shown an</p> <p>18 association. We know that's not true. There</p> <p>19 have been some. So there is some evidence. It's</p> <p>20 the totality of the evidence that I don't</p> <p>21 believe.</p> <p>22 MS. THOMPSON:</p> <p>23 Q Okay.</p> <p>24 A But it would not be unreasonable for</p>	<p style="text-align: right;">Page 161</p> <p>1 you will agree?</p> <p>2 A 2010?</p> <p>3 Q 2001.</p> <p>4 A 2001. Uh-huh. Yeah. Okay.</p> <p>5 Q Are you aware of anything that</p> <p>6 Johnson & Johnson did in 2001 to address this</p> <p>7 idea of Dr. Balkwill and others, including</p> <p>8 Dr. Ness, that talc may be causing ovarian cancer</p> <p>9 through an inflammatory process?</p> <p>10 MS. CURRY:</p> <p>11 Object to the form.</p> <p>12 A In 2000 -- in 2001?</p> <p>13 MS. THOMPSON:</p> <p>14 Q Right.</p> <p>15 Did Johnson & Johnson respond to what</p> <p>16 at least is reported as being in the literature</p> <p>17 in Lancet?</p> <p>18 MS. CURRY:</p> <p>19 Object to the form.</p> <p>20 A I'm not aware of that.</p> <p>21 MS. THOMPSON:</p> <p>22 Q I'm gonna mark as Exhibit 13 --</p> <p>23 MS. EVERETT:</p> <p>24 12.</p>

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<p>1 MS. THOMPSON: 2 Q Oh, there it is. 3 (DEPOSITION EXHIBIT NUMBER 12 4 WAS MARKED FOR IDENTIFICATION.) 5 MS. THOMPSON: 6 Q Exhibit 12 is going to be another 7 article -- another review article by Dr. Reuter 8 and authors. Oh, we need to -- sorry. Make sure 9 that's not my copy. 10 A This is mine? 11 Q That's yours, yeah. 12 Are you familiar with the journal of 13 Free Radical Biology in Medicine? 14 A I am familiar. Not something I publish 15 in much. 16 Q And probably doesn't have quite the 17 reputation of The Lancet or Cell? 18 A I don't think so. 19 Q But regardless, it's peer-reviewed. 20 A Uh-huh. 21 Q Are you familiar with any of these 22 authors? 23 A Not firsthand. Aggarwal I may have 24 heard about, but not, firsthand, no.</p>	<p>1 A Where are you now? 2 Q I'm turning to page 2, 1604 in the 3 introduction section. 4 A Uh-huh. 5 Q The second paragraph reads "Under a 6 sustained environmental stress, ROS -- R-O-S -- 7 are produced over a long time, and thus 8 significant damage may occur to cell structure 9 and functions and may induce somatic mutations 10 and neoplastic transformation. 11 "Indeed, cancer initiation and 12 progression have been linked to oxidative stress 13 by increasing DNA mutations or inducing DNA 14 damage, genome instability, and cell 15 proliferation." 16 Would you agree with that sentence in a 17 general sense? 18 MS. CURRY: 19 Object to the form. 20 A I'm just looking at the references. 21 MS. THOMPSON: 22 Q And take a moment if you need to do 23 that. 24 A Sure.</p>
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<p>1 Q And reading -- and the title of this 2 review article is "Oxidative stress, 3 inflammation, and cancer. How are they linked?" 4 Right? 5 A Correct. 6 Q Reading in the abstract, the last 7 couple of sentences starting with "How oxidative 8 stress activates inflammatory pathways leading to 9 a transformation of a normal cell to tumor cell, 10 tumor cell survival, proliferation, 11 chemoresistance, radioresistance, invasion, 12 angiogenesis, and stem cell survival is the focus 13 of this review. Overall, observations to date 14 suggest that oxidative stress, chronic 15 inflammation, and cancer are closely linked." 16 Would you agree with that statement? 17 MS. CURRY: 18 Object to the form. 19 A Yes. 20 MS. THOMPSON: 21 Q In a general sense, in a review 22 article? 23 A Correct. 24 Q And --</p>	<p>1 I think as a general statement, I 2 wouldn't -- I would not disagree with that. I 3 think that's -- yeah. 4 Q Sorry. 5 A Go ahead. 6 Q And this article was published in 2010; 7 correct? 8 A Correct. 9 Q And looking at Table 2, a partial list 10 of cancers that have been linked to reactive 11 oxygen species, and under that list is ovarian 12 cancer. 13 Would you agree that in 2010 ovarian 14 cancer had been linked to reactive oxygen 15 species? 16 MS. CURRY: 17 Object to the form. 18 A Yeah. This was a little more 19 complicated in the sense I'm not sure why every 20 case was not listed because reactive oxygen 21 species are present in essentially every cell in 22 the body. So it's a -- it's an odd table in that 23 it's a subset and then -- it's sort of implying 24 reactive oxygen species are not important in</p>

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<p style="text-align: right;">Page 166</p> <p>1 other cancers.</p> <p>2 And, then, too, what they reference is</p> <p>3 51, which is a really odd reference. "Loss of</p> <p>4 Mkp3 mediated by oxidative stress enhances tumor</p> <p>5 genicity and chemoresistance of ovarian cancer</p> <p>6 cells."</p> <p>7 Hardly a paper -- I mean, I'm</p> <p>8 extrapolating the title. Hardly a paper that</p> <p>9 would say that reactive oxygen species is</p> <p>10 critical to the development of ovarian cancer.</p> <p>11 That's chemoresistance. That's -- that's at the</p> <p>12 end of natural history, so...</p> <p>13 MS. THOMPSON:</p> <p>14 Q But at least the authors in this</p> <p>15 peer-reviewed review article thought appropriate</p> <p>16 to list ovarian cancer under one of the cancers</p> <p>17 that have been linked to reactive oxygen species;</p> <p>18 right?</p> <p>19 A It's there.</p> <p>20 (DEPOSITION EXHIBIT NUMBER 13</p> <p>21 WAS MARKED FOR IDENTIFICATION.)</p> <p>22 MS. THOMPSON:</p> <p>23 Q I'm marking as Exhibit 13 another</p> <p>24 review article from Lancet. This one, a little</p>	<p style="text-align: right;">Page 168</p> <p>1 Object to the form.</p> <p>2 A Oza and Vergote are -- Vergote is a</p> <p>3 surgeon and very much clinical. I don't think he</p> <p>4 does any work in the lab. Oza is developmental</p> <p>5 therapeutics clinical. Charlie is the scientist</p> <p>6 here.</p> <p>7 MS. THOMPSON:</p> <p>8 Q Okay. And I think --</p> <p>9 A Yeah.</p> <p>10 Q -- at least with this review article,</p> <p>11 it was meant to address --</p> <p>12 A Everything.</p> <p>13 Q -- all -- all aspects --</p> <p>14 A Right.</p> <p>15 Q -- from my reading of it.</p> <p>16 A And I think Stephanie works for Amit, I</p> <p>17 think.</p> <p>18 Q So these are well-regarded --</p> <p>19 A Uh-huh.</p> <p>20 Q -- scientists and experts in ovarian</p> <p>21 cancer. You would agree?</p> <p>22 MS. CURRY:</p> <p>23 Object to the form.</p> <p>24 A Yes.</p>
<p style="text-align: right;">Page 167</p> <p>1 more current.</p> <p>2 Have you seen this article, Dr. Birrer?</p> <p>3 A I know the -- I know the authors, but I</p> <p>4 haven't actually --</p> <p>5 Q Oh. Did I give you a highlighted --</p> <p>6 A I -- I don't think so.</p> <p>7 Q Okay.</p> <p>8 A It would be helpful if it was</p> <p>9 highlighted.</p> <p>10 Q It would be helpful to me also.</p> <p>11 That's okay.</p> <p>12 And, in fact, these -- I think three of</p> <p>13 the four authors you have published with. Does</p> <p>14 that sound right?</p> <p>15 A Ignace, Charlie, Amit, I know all of</p> <p>16 them. I don't know Stephanie.</p> <p>17 Q I think that was the one that I did not</p> <p>18 see on -- on your CV as one of your coauthors.</p> <p>19 And this review article -- and you</p> <p>20 would assume that -- well, we don't have to</p> <p>21 assume -- are Dr. Gourley, Dr. Vergote and</p> <p>22 Dr. Oza considered experts in the field of</p> <p>23 epithelial ovarian cancer?</p> <p>24 MS. CURRY:</p>	<p style="text-align: right;">Page 169</p> <p>1 MS. THOMPSON:</p> <p>2 Q And this is a review article, as we</p> <p>3 said, just published in Lancet within -- March</p> <p>4 23rd, so within the last week.</p> <p>5 Have you seen this article?</p> <p>6 A This one?</p> <p>7 Q Yes.</p> <p>8 A No. Just the last week.</p> <p>9 Q Let's look in the first section,</p> <p>10 Epidemiology and Risk Factors. And the last</p> <p>11 sentence, "Risk factors for EOC include the</p> <p>12 number of lifetime of ovulations (absence of</p> <p>13 pregnancy), early age of menarche and late age at</p> <p>14 menopause, family history of EOC, smoking, benign</p> <p>15 gynecological conditions, including</p> <p>16 endometriosis -- endometriosis, polycystic ovary</p> <p>17 disease and pelvic inflammatory disease, and</p> <p>18 potentially use of talcum powder."</p> <p>19 Would you agree that at least the</p> <p>20 authors thought that the use of talcum powder is</p> <p>21 potentially a risk factor for EOC?</p> <p>22 MS. CURRY:</p> <p>23 Object to the form.</p> <p>24 A And, again, this is a review. So I</p>

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<p>1 think they're trying to be inclusive. And I</p> <p>2 don't actually know that any of them believe</p> <p>3 that.</p> <p>4 MS. THOMPSON:</p> <p>5 Q So would -- would they -- would they</p> <p>6 have -- would it be the two options again, either</p> <p>7 they're wrong --</p> <p>8 A (Nods affirmatively.)</p> <p>9 Q -- or that they're just reporting on</p> <p>10 what the literature states?</p> <p>11 A (Nods affirmatively.)</p> <p>12 MS. CURRY:</p> <p>13 Object to the form.</p> <p>14 A Yeah. I think it extends beyond</p> <p>15 talcum, too, to be honest with you. I don't -- I</p> <p>16 don't consider smoking to be a strong risk for</p> <p>17 ovarian cancer. And PID, I don't either.</p> <p>18 So -- and I don't know of many of my --</p> <p>19 I mean, we don't -- we don't want our patients</p> <p>20 smoking. But I don't know of many of the</p> <p>21 gynecologic oncologists I work with who -- that's</p> <p>22 on their -- that's on their risk list.</p> <p>23 MS. THOMPSON:</p> <p>24 Q Even for mucinous?</p>	<p>1 Q So the authors, if they were reporting</p> <p>2 on the potential risk of talcum powder use in</p> <p>3 ovarian cancer chose to cite Penninkilampi as a</p> <p>4 source -- as the source for that information;</p> <p>5 correct?</p> <p>6 A They reference it.</p> <p>7 Q And you would assume they would choose</p> <p>8 the most authoritative article that was available</p> <p>9 in the literature?</p> <p>10 MS. CURRY:</p> <p>11 Object to the form.</p> <p>12 MS. THOMPSON:</p> <p>13 Q Wouldn't you?</p> <p>14 A I would not assume that.</p> <p>15 Q You would assume they'd pick something</p> <p>16 that wasn't as authoritative? There's something</p> <p>17 else they could have picked?</p> <p>18 MS. CURRY:</p> <p>19 Object to the form.</p> <p>20 A They may have -- they may have picked</p> <p>21 that because it was one of the more recent</p> <p>22 meta-analyses, and so it was convenient. And</p> <p>23 it's flawed. We can go over if you'd like.</p> <p>24 MS. THOMPSON:</p>
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<p>1 A Well, now you're gonna get complicated</p> <p>2 on me because, you know, there are people that</p> <p>3 don't think -- there are mucinous tumors of the</p> <p>4 ovary. Bob Kirkman is one of them, and that is</p> <p>5 all GI.</p> <p>6 So I think -- I don't think it's all</p> <p>7 that relevant because it's such a rare tumor.</p> <p>8 Q And the citation for the reference</p> <p>9 that --</p> <p>10 A 8?</p> <p>11 Q -- a risk factor potentially would --</p> <p>12 could be the use of talcum powder is the</p> <p>13 Penninkilampi meta-analysis; right?</p> <p>14 A That's referenced in 8, yes.</p> <p>15 Q So at least the authors, the reviewers,</p> <p>16 the editors of the journal felt that the most</p> <p>17 authoritative source would be that Penninkilampi</p> <p>18 meta-analysis. Would you agree?</p> <p>19 MS. CURRY:</p> <p>20 Object to the form.</p> <p>21 A Say that again. I'm sorry.</p> <p>22 MS. THOMPSON:</p> <p>23 Q Yeah.</p> <p>24 A I could read it.</p>	<p>1 Q Well, I'm just saying these authors</p> <p>2 picked that to -- to support the statement in</p> <p>3 their review article in The Lancet that the use</p> <p>4 of talcum powder is potentially a risk factor for</p> <p>5 ovarian cancer.</p> <p>6 A Well, I would agree that they picked</p> <p>7 that reference. I disagree that that's because</p> <p>8 they thought it was the most authoritative</p> <p>9 article. It is one of the more recent, and, so,</p> <p>10 therefore, a lot of the other papers would be</p> <p>11 included in it. So it's a convenient place to</p> <p>12 steer a reader.</p> <p>13 Q Do you think they'd pick it if they</p> <p>14 thought it was flawed?</p> <p>15 MS. CURRY:</p> <p>16 Object to the form.</p> <p>17 A Probably if -- if it was seriously</p> <p>18 flawed, I don't think they would have picked it.</p> <p>19 Yeah.</p> <p>20 MS. THOMPSON:</p> <p>21 Q And would you agree, also, that the</p> <p>22 reviewers would not have included an article that</p> <p>23 the reviewers felt was seriously flawed?</p> <p>24 MS. CURRY:</p>

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<p>1 Object to the form.</p> <p>2 A Again, it's a little bit -- having been</p> <p>3 involved in these processes, to be perfectly</p> <p>4 frank, you get a review article with a review of</p> <p>5 147 references, you're not gonna go through them</p> <p>6 all. So I don't know I can say with any</p> <p>7 authority that the reviewers looked at this and</p> <p>8 said, gee, they picked the one talc paper that is</p> <p>9 really spectacular.</p> <p>10 MS. THOMPSON:</p> <p>11 Q Okay. So there were -- but there --</p> <p>12 there were no --</p> <p>13 A The review, and -- and it's true for</p> <p>14 the editor too.</p> <p>15 Q Okay. So at least there were no red</p> <p>16 flags in front of the reviewers and the editor</p> <p>17 when they saw the Penninkilampi article cited for</p> <p>18 that reference?</p> <p>19 MS. CURRY:</p> <p>20 Object to the form.</p> <p>21 A I --</p> <p>22 MS. THOMPSON:</p> <p>23 Q That would cause them to --</p> <p>24 A I don't know they noticed it.</p>	<p>1 lunch?</p> <p>2 MS. CURRY:</p> <p>3 We actually did order in lunch. I'm</p> <p>4 not sure if we -- if you want to take a quick</p> <p>5 break, I can check on the estimated time of</p> <p>6 arrival.</p> <p>7 MS. THOMPSON:</p> <p>8 Sure. Or we can just keep going until</p> <p>9 we get word. Whatever --</p> <p>10 A Or we could just finish.</p> <p>11 MR. MIZGALA:</p> <p>12 I second that.</p> <p>13 MS. GARBER:</p> <p>14 You guys keep going. I'll check.</p> <p>15 MS. THOMPSON:</p> <p>16 Are you telling me you're not having</p> <p>17 fun? I think he liked the test.</p> <p>18 THE WITNESS:</p> <p>19 Yeah. It would have been nice to have</p> <p>20 the little box -- the little circles you could</p> <p>21 fill in. You know.</p> <p>22 MS. THOMPSON:</p> <p>23 And then I could just put it in the</p> <p>24 computer.</p>
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<p>1 Q Okay. But the editors selected that</p> <p>2 article; correct?</p> <p>3 MS. CURRY:</p> <p>4 Object to the form.</p> <p>5 MS. THOMPSON:</p> <p>6 Q For whatever reason?</p> <p>7 A The --</p> <p>8 Q The authors.</p> <p>9 A The authors selected it.</p> <p>10 Q Sorry.</p> <p>11 A Not -- not the editors. Correct.</p> <p>12 Q Thank you. I meant to say authors.</p> <p>13 A And, again, I would just emphasize it</p> <p>14 says "potentially use of talcum powder."</p> <p>15 Q That's right.</p> <p>16 A Okay.</p> <p>17 Q And at least in this statement, the</p> <p>18 reference to talcum powder as potentially a risk</p> <p>19 factor did not separate out the subtypes. It's</p> <p>20 referring to EOC; correct?</p> <p>21 A I -- that's the way I would read it,</p> <p>22 right.</p> <p>23 MS. THOMPSON:</p> <p>24 Dawn, what are you thinking about</p>	<p>1 THE WITNESS:</p> <p>2 No mumbling? Sorry.</p> <p>3 MS. CURRY:</p> <p>4 Okay. So the lunch, I was just told,</p> <p>5 is actually here. So it's up to you when you're</p> <p>6 in a good breaking point.</p> <p>7 MS. THOMPSON:</p> <p>8 Dr. Birrer, do you want to take a break</p> <p>9 for lunch or do you want to go another 15 or 20</p> <p>10 minutes?</p> <p>11 THE WITNESS:</p> <p>12 Going would be fine.</p> <p>13 MS. THOMPSON:</p> <p>14 Q Okay.</p> <p>15 A Yeah.</p> <p>16 Q Let's -- let's look at the IARC 93, the</p> <p>17 one that --</p> <p>18 A Uh-huh.</p> <p>19 Q -- addresses the nonasbestiform talc.</p> <p>20 And turning to page 277 in the exposure data</p> <p>21 introduction --</p> <p>22 A Uh-huh. Do you want to use mine?</p> <p>23 Q Let's have a blank one to follow along.</p> <p>24 Does this section define the</p>

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<p style="text-align: right;">Page 178</p> <p>1 nonasbestiform talc?</p> <p>2 MS. CURRY:</p> <p>3 Object to the form.</p> <p>4 MS. THOMPSON:</p> <p>5 Q Oh, there it is. And let's just read</p> <p>6 along in that third paragraph.</p> <p>7 A Okay.</p> <p>8 Q "Asbestiform talc fibers are very long</p> <p>9 and thin and occur in parallel bundles that are</p> <p>10 easily separated from one another by hand</p> <p>11 pressure." And asbestos -- no. Just strike</p> <p>12 that.</p> <p>13 You're -- you're not an expert in the</p> <p>14 different types of asbestos or talc in its</p> <p>15 different --</p> <p>16 A I'm learning --</p> <p>17 Q Are you?</p> <p>18 A I'm learning a lot.</p> <p>19 Q I -- well, I don't want to ask those</p> <p>20 questions to you later because then you'll be an</p> <p>21 expert.</p> <p>22 Let's -- let's go to the conclusions of</p> <p>23 IARC. We've already established that IARC used a</p> <p>24 pretty extensive methodology in reaching their</p>	<p style="text-align: right;">Page 180</p> <p>1 was -- well, that there was limited evidence in</p> <p>2 humans for the carcinogenicity in peroneal use of</p> <p>3 talcum powder body product. Is that what IARC</p> <p>4 concluded?</p> <p>5 A That's in 6.1, the second one. Yes.</p> <p>6 Q Right.</p> <p>7 And there is limited evidence in</p> <p>8 experimental animals; right?</p> <p>9 A 6.2. Yes.</p> <p>10 Q And in the rationale, the authors</p> <p>11 state, third paragraph, "For peroneal use of</p> <p>12 talcum-based body power, many case-control</p> <p>13 studies of ovarian cancer found a modest but an</p> <p>14 unusually consistent excessive risk, although the</p> <p>15 impact of bias and potential confounding could</p> <p>16 not be ruled out."</p> <p>17 Is -- is that your understanding of the</p> <p>18 conclusions?</p> <p>19 A That's what they concluded.</p> <p>20 Q And --</p> <p>21 A We're done with IARC?</p> <p>22 Q We're done with IARC.</p> <p>23 And you also looked at the Health</p> <p>24 Canada Assessment; right?</p>
<p style="text-align: right;">Page 179</p> <p>1 conclusions; right?</p> <p>2 MS. CURRY:</p> <p>3 Object to the form.</p> <p>4 A Yes.</p> <p>5 MS. THOMPSON:</p> <p>6 Q And in your -- in your opinion, IARC</p> <p>7 got -- got it wrong; right?</p> <p>8 MS. CURRY:</p> <p>9 Object to the form.</p> <p>10 A I think the net -- and I -- let me just</p> <p>11 summarize. I agree that they did a thorough sort</p> <p>12 of process here. In the end, what they</p> <p>13 concluded, I think, was -- was wrong. If I</p> <p>14 recall correctly, it's 2B.</p> <p>15 MS. THOMPSON:</p> <p>16 Q That's right.</p> <p>17 A Was the classification.</p> <p>18 Q But 2B does not mean that it's not</p> <p>19 carcinogenic, does it?</p> <p>20 A Means it's possible carcinogenic. I</p> <p>21 think that's by definition.</p> <p>22 Q Right.</p> <p>23 And -- and in this situation, the</p> <p>24 reason for the classification was that there</p>	<p style="text-align: right;">Page 181</p> <p>1 A Yes.</p> <p>2 Q And we agreed that the methodology that</p> <p>3 Health Canada applied for -- for their</p> <p>4 determination was also extensive; right?</p> <p>5 MS. CURRY:</p> <p>6 Object to the form.</p> <p>7 A They were systematic and thorough. I</p> <p>8 think it was pretty complicated, yeah.</p> <p>9 MS. THOMPSON:</p> <p>10 Q And what's your understanding of the</p> <p>11 conclusions reached by the -- Health Canada?</p> <p>12 MS. CURRY:</p> <p>13 Object to the form.</p> <p>14 MS. THOMPSON:</p> <p>15 Q Scientists.</p> <p>16 A Well, they concluded that there was a</p> <p>17 low risk of harm to the environment from talc.</p> <p>18 Q Is that what you came away with?</p> <p>19 A Well, it was in the third paragraph.</p> <p>20 So it was important to note that. But they did</p> <p>21 conclude that talc meets one of the criteria.</p> <p>22 That was Section 64. And so they concluded that</p> <p>23 it potentially presented a health risk to</p> <p>24 Canadians, if I got that right.</p>

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<p>1 Q And do you think it was just to</p> <p>2 Canadians?</p> <p>3 A Well, that's the way they quoted it.</p> <p>4 Q And --</p> <p>5 A In fact, the statement is "may</p> <p>6 constitute a danger in Canada to health" --</p> <p>7 "human health" -- "human life or health."</p> <p>8 Q And they also made the -- well, let's</p> <p>9 read beginning on page little -- little 3, i --</p> <p>10 iii?</p> <p>11 A I'm sorry. Where are you?</p> <p>12 Q Little -- little roman numeral 3.</p> <p>13 A Three? Yeah.</p> <p>14 Q Is your understanding that the -- that</p> <p>15 Health Canada found that the available data were</p> <p>16 indicative of a causal effect?</p> <p>17 A Where are you reading?</p> <p>18 Q I was just asking you what your</p> <p>19 understanding was.</p> <p>20 MS. CURRY:</p> <p>21 Object to the form.</p> <p>22 A I'm not sure that they actually found</p> <p>23 causal effects.</p> <p>24 MS. THOMPSON:</p>	<p>1 Q -- executive summary.</p> <p>2 A Yeah. Uh-huh.</p> <p>3 Q "Given that there is potential for</p> <p>4 peroneal exposure to talc from the use of various</p> <p>5 self-care products, for example, body powder,</p> <p>6 baby powder, diaper and rash creams, gentle</p> <p>7 antiperspirants and deodorants, body wipes, bath</p> <p>8 bombs, a potential concern for human health has</p> <p>9 been identified."</p> <p>10 Correct?</p> <p>11 A I agree with that.</p> <p>12 Q And is it your opinion that Health</p> <p>13 Canada got it wrong also?</p> <p>14 MS. CURRY:</p> <p>15 Object to the form.</p> <p>16 A So it's interesting. When I reviewed</p> <p>17 this was -- again, this is a very recent -- looks</p> <p>18 like December 2018 -- decision by Health Canada</p> <p>19 based upon a huge body of literature, which I had</p> <p>20 reviewed and come to a different conclusion.</p> <p>21 So there really was not very much new</p> <p>22 data to draw this conclusion. So, you know,</p> <p>23 again, I think very much like IARC, I think they</p> <p>24 got it wrong.</p>
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<p>1 Q Okay. Well, let's -- let's read</p> <p>2 beginning -- the paragraph with "The</p> <p>3 meta-analyses."</p> <p>4 A Where are you? Oh, the -- yeah.</p> <p>5 Q "The meta-analyses of the available</p> <p>6 human studies in the peer-reviewed literature" --</p> <p>7 A Yep.</p> <p>8 Q -- "indicate a statistically</p> <p>9 significant positive association between perineal</p> <p>10 exposure to talc and ovarian cancer. Further,</p> <p>11 available data are indicative of a causal</p> <p>12 effect."</p> <p>13 A Uh-huh.</p> <p>14 Q So they did --</p> <p>15 A (Nods affirmatively.)</p> <p>16 Q -- determine that it was indicative of</p> <p>17 a causal effect; right?</p> <p>18 MS. CURRY:</p> <p>19 Object to the form.</p> <p>20 A That's what they said, yes. It's not</p> <p>21 referenced, but --</p> <p>22 MS. THOMPSON:</p> <p>23 Q Well, this is the --</p> <p>24 A Yeah.</p>	<p>1 MS. THOMPSON:</p> <p>2 Q And you don't think that this is a</p> <p>3 situation where scientists can look at the same</p> <p>4 data and -- and make different conclusions?</p> <p>5 A No.</p> <p>6 MS. CURRY:</p> <p>7 Object to the form.</p> <p>8 MS. THOMPSON:</p> <p>9 Q Do you have any reason to believe that</p> <p>10 the scientists who worked on this project were</p> <p>11 unreasonable?</p> <p>12 MS. CURRY:</p> <p>13 Object to the form.</p> <p>14 A Other than the fact they drew the wrong</p> <p>15 conclusion here, I know nothing else about them,</p> <p>16 so...</p> <p>17 MS. THOMPSON:</p> <p>18 Q You don't have any reason to believe</p> <p>19 they were incompetent?</p> <p>20 MS. CURRY:</p> <p>21 Object to the form.</p> <p>22 A No.</p> <p>23 MS. THOMPSON:</p> <p>24 Q Do you have any reason to believe that</p>

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<p>1 they weren't good scientists?</p> <p>2 MS. CURRY:</p> <p>3 Object to the form.</p> <p>4 A I don't really have a lot of knowledge</p> <p>5 of them. If I could actually find the list of</p> <p>6 individuals who made this decision -- I don't</p> <p>7 think it's published.</p> <p>8 MS. THOMPSON:</p> <p>9 Q And did you -- this was done under the</p> <p>10 auspices, I believe, of the Minister of Health.</p> <p>11 A Uh-huh.</p> <p>12 Q You don't know the Minister of Health</p> <p>13 in Canada, do you?</p> <p>14 A I don't.</p> <p>15 Q Or know that he would -- or she would</p> <p>16 not be competent?</p> <p>17 MS. CURRY:</p> <p>18 Object to the form.</p> <p>19 A I have no direct evidence for that.</p> <p>20 MS. THOMPSON:</p> <p>21 Q Do you take any issue with the weight</p> <p>22 of the evidence methodology that Health Canada</p> <p>23 applied?</p> <p>24 A No.</p>	<p>1 A In terms of peer review, scientific</p> <p>2 peer review?</p> <p>3 Q Correct.</p> <p>4 A I can't say that definitively.</p> <p>5 Q If you'll look at the -- and the copy</p> <p>6 that I'm looking at doesn't have page numbers, so</p> <p>7 that's why it's -- I'm --</p> <p>8 A Roughly.</p> <p>9 Q -- making it difficult.</p> <p>10 But if you look at the big bold</p> <p>11 introduction that comes right after the synopsis,</p> <p>12 it should be about the -- it may be the little</p> <p>13 numbers.</p> <p>14 A Introduction?</p> <p>15 Q Yeah.</p> <p>16 And the very bottom of that page, I'm</p> <p>17 reading "The human health portion of this</p> <p>18 assessment has undergone external peer review</p> <p>19 and/or consultation?"</p> <p>20 Doesn't -- does the assessment, at</p> <p>21 least, state that it underwent peer review and</p> <p>22 consultation?</p> <p>23 A It states that. I don't quite -- I</p> <p>24 don't honestly know what that means.</p>
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<p>1 Q Only that they came up with the wrong</p> <p>2 conclusion; right?</p> <p>3 A Correct.</p> <p>4 Q And this assessment, like IARC, was</p> <p>5 based on talc -- cosmetic-grade talc and not on</p> <p>6 potential impurities such as asbestos. Is that</p> <p>7 also your understanding?</p> <p>8 MS. CURRY:</p> <p>9 Object to the form.</p> <p>10 A That is my understanding. So, you</p> <p>11 know, again, it's -- it's the same epi data. The</p> <p>12 epi data is focused on talcum powder. So that --</p> <p>13 that applies here, too.</p> <p>14 MS. THOMPSON:</p> <p>15 Q And is it your understanding that the</p> <p>16 human health portion of the Health Canada</p> <p>17 assessment went through a peer-review process?</p> <p>18 MS. CURRY:</p> <p>19 Object to the form.</p> <p>20 MS. THOMPSON:</p> <p>21 Q With external reviewers.</p> <p>22 A I didn't see that described.</p> <p>23 Q So you don't know one way or the other</p> <p>24 whether it went through a review process?</p>	<p>1 Q Okay.</p> <p>2 A And the public comment period, of</p> <p>3 course, is just a governmental response.</p> <p>4 Q Do you know if Johnson & Johnson has</p> <p>5 submitted comments to Health Canada?</p> <p>6 MS. CURRY:</p> <p>7 Object to the form.</p> <p>8 A Not that I know of.</p> <p>9 MS. THOMPSON:</p> <p>10 Q Have you submitted comments to Health</p> <p>11 Canada --</p> <p>12 A No.</p> <p>13 Q -- with your opinions?</p> <p>14 A No.</p> <p>15 Q Do you intend to submit any opinions to</p> <p>16 Health Canada?</p> <p>17 A I doubt it.</p> <p>18 Q You are -- are you aware that talc used</p> <p>19 as a dry powder lubricant on condoms was</p> <p>20 substituted with cornstarch in the 1990s?</p> <p>21 A I believe I am familiar with that.</p> <p>22 Q Do you know why?</p> <p>23 A No.</p> <p>24 Q Do you know that dusting diaphragms,</p>

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<p style="text-align: right;">Page 190</p> <p>1 the practice of dusting diaphragms with talcum</p> <p>2 powder was abandoned approximately the same time?</p> <p>3 MS. CURRY:</p> <p>4 Object to the form.</p> <p>5 A Yes.</p> <p>6 MS. THOMPSON:</p> <p>7 Q Do you know why?</p> <p>8 A No.</p> <p>9 Q Was it for concerns about inflammatory</p> <p>10 and cancer effects?</p> <p>11 MS. CURRY:</p> <p>12 Object to the form.</p> <p>13 A Could have been. I don't -- can't</p> <p>14 quote that.</p> <p>15 MS. THOMPSON:</p> <p>16 Q Were you aware that FDA banned -- has</p> <p>17 banned powder examination and surgical gloves?</p> <p>18 A Yes.</p> <p>19 Q Do you know why?</p> <p>20 A That was based upon the concern about</p> <p>21 the generation of fibrosis.</p> <p>22 Q And other inflammatory processes in</p> <p>23 the -- in the peritoneal cavity?</p> <p>24 MS. CURRY:</p>	<p style="text-align: right;">Page 192</p> <p>1 Q Are you aware of the differences</p> <p>2 between cornstarch and talc?</p> <p>3 MS. CURRY:</p> <p>4 Object to the form.</p> <p>5 A In terms of biochemical and physical</p> <p>6 differences?</p> <p>7 MS. THOMPSON:</p> <p>8 Q Sure. Let's start there.</p> <p>9 A Yeah. I don't think I can list them</p> <p>10 all. But certainly cornstarch is a biologic</p> <p>11 agent, it's a carbohydrate, and talc is a</p> <p>12 mineral.</p> <p>13 We've already talked a little bit about</p> <p>14 the size of particles in talcum powder and it's</p> <p>15 exceedingly variable. So it's a little hard to</p> <p>16 compare those two particles. But I would think</p> <p>17 that starch would be more homogeneous and of a</p> <p>18 different size.</p> <p>19 And then, you know, biochemical</p> <p>20 differences are substantial. I mean, this is a</p> <p>21 carbohydrate, which can be broken down by certain</p> <p>22 enzymes, has, you know, a firm structure to it.</p> <p>23 Talc, as a mineral, forms suspensions.</p> <p>24 It is not soluble. Starch is more soluble. So</p>
<p style="text-align: right;">Page 191</p> <p>1 Object to the form.</p> <p>2 A I would define -- I would define that</p> <p>3 as fibrosis, if not inflammatory.</p> <p>4 MS. THOMPSON:</p> <p>5 Q Do you consider granulomas an</p> <p>6 inflammatory response?</p> <p>7 A It's in the characterization of chronic</p> <p>8 inflammation, yes.</p> <p>9 Q Are adhesions an inflammatory response?</p> <p>10 A Not necessarily.</p> <p>11 Q And they would be an acute response</p> <p>12 if -- if they were caused by an inflammatory</p> <p>13 reaction?</p> <p>14 MS. CURRY:</p> <p>15 Object to the form.</p> <p>16 A So adhesions are, you know, essentially</p> <p>17 scar tissue and fibrosis. The etiology of it is</p> <p>18 pretty broad. Some of it could be chronic</p> <p>19 inflammation. Some of it could be acute</p> <p>20 inflammation. And I would not even rule out the</p> <p>21 possibility that general wound healing would give</p> <p>22 rise to scar tissue. And that may not</p> <p>23 necessarily fit the criteria of inflammation.</p> <p>24 MS. THOMPSON:</p>	<p style="text-align: right;">Page 193</p> <p>1 there's differences.</p> <p>2 Q So, in general terms, cornstarch would</p> <p>3 typically be absorbed or metabolized by the body?</p> <p>4 MS. CURRY:</p> <p>5 Object to the form.</p> <p>6 MS. THOMPSON:</p> <p>7 Q Would you agree?</p> <p>8 A Absorbed or -- there's -- it would</p> <p>9 certainly be more likely, I think, than a</p> <p>10 mineral, yeah.</p> <p>11 Q Whereas the mineral, once it's there,</p> <p>12 is expected to remain there; correct?</p> <p>13 MS. CURRY:</p> <p>14 Object to the form.</p> <p>15 A It's a little hard to tell because then</p> <p>16 there are other mechanisms remove particulate</p> <p>17 matters; right? So macrophages come along and</p> <p>18 they phagocytize them. That macrophage then may</p> <p>19 travel somewhere else and then essentially</p> <p>20 deposit it in a way that the mineral -- the</p> <p>21 mineral particle could be removed. So -- so it's</p> <p>22 a little bit complex.</p> <p>23 MS. THOMPSON:</p> <p>24 Q Can inhaled talc particles appear in</p>

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<p style="text-align: right;">Page 194</p> <p>1 distant organs?</p> <p>2 A So there is some data, I believe, in</p> <p>3 animal studies that high concentrations of talc,</p> <p>4 either in the pleural cavity or in intratracheal</p> <p>5 injections can end up in what --</p> <p>6 And I think I put them in the expert</p> <p>7 report; for instance, the spleen.</p> <p>8 Q And ovaries? Can they occur in the</p> <p>9 ovaries?</p> <p>10 A So if you look at the literature -- you</p> <p>11 know, and I went through in pretty big detail --</p> <p>12 nobody's looked. So there's no reproductive</p> <p>13 organs in any of those studies. At least the</p> <p>14 ones that I have looked at. So I don't think we</p> <p>15 know, and I don't think we could assume that.</p> <p>16 Q Can talc fibers enter the peritoneal</p> <p>17 cavity?</p> <p>18 MS. CURRY:</p> <p>19 Object to the form.</p> <p>20 A Again, we're back to this mineral</p> <p>21 structure, and I'm not going to be able to</p> <p>22 comment on that.</p> <p>23 MS. THOMPSON:</p> <p>24 Q And how about asbestos fibers?</p>	<p style="text-align: right;">Page 196</p> <p>1 know that.</p> <p>2 Q So you know -- you -- we know that</p> <p>3 asbestos fibers can reach the peritoneal cavity;</p> <p>4 correct?</p> <p>5 A Yes.</p> <p>6 Q And -- and let me just understand</p> <p>7 you -- what you're opining today is that we just</p> <p>8 don't know how they get there?</p> <p>9 MS. CURRY:</p> <p>10 Object to the form.</p> <p>11 A I don't know. So -- so I think one of</p> <p>12 the hypotheses that -- after asbestos -- again,</p> <p>13 I'm not -- I wasn't asked to explore asbestos in</p> <p>14 great detail. This is more my medical training</p> <p>15 speaking.</p> <p>16 But as people inhaled asbestos, these</p> <p>17 particles would work their way out into the</p> <p>18 pleural cavity --</p> <p>19 MS. THOMPSON:</p> <p>20 Q So --</p> <p>21 A -- which is where they would do their</p> <p>22 badness. And then, there is a hypothesis</p> <p>23 connection between the pleural cavity and the</p> <p>24 peritoneal cavity.</p>
<p style="text-align: right;">Page 195</p> <p>1 A Well, asbestos exposure can, of course,</p> <p>2 give rise to mesothelioma and can give rise to</p> <p>3 peritoneal mesotheliomas. So it's got to get</p> <p>4 there from somewhere.</p> <p>5 Q Do you have an opinion as to whether</p> <p>6 asbestos fibers can get to the peritoneal cavity</p> <p>7 through peritoneal exposure and migration through</p> <p>8 the genital tract?</p> <p>9 MS. CURRY:</p> <p>10 Object to the form.</p> <p>11 A I don't have any data on that.</p> <p>12 MS. THOMPSON:</p> <p>13 Q So you have no opinion.</p> <p>14 A I would say analogous with the</p> <p>15 migration data that there's not a lot of evidence</p> <p>16 things are migrating retrograde. So -- and I</p> <p>17 think -- although I don't think those experiments</p> <p>18 have been done with asbestos in mind -- and we</p> <p>19 know that asbestos can travel with high</p> <p>20 insulation [sic] -- you know, inhalation of</p> <p>21 asbestos can get in the pleural cavity. It gets</p> <p>22 there from somewhere. It's got to be inside the</p> <p>23 lung. It has to get out in the pleural cavity,</p> <p>24 and then again, the peritoneal cavity. So we</p>	<p style="text-align: right;">Page 197</p> <p>1 Q So direct penetration of the fiber</p> <p>2 through the pleura?</p> <p>3 A The diaphragm's are pretty secure</p> <p>4 structures, so it's a little bit -- I can't say,</p> <p>5 hey, here's the pathway. But that's the</p> <p>6 supposition.</p> <p>7 Q Okay.</p> <p>8 A Okay.</p> <p>9 Q Do you -- are you aware of any</p> <p>10 epidemiologic or other studies that have linked</p> <p>11 the use of perineal cornstarch with ovarian</p> <p>12 cancer?</p> <p>13 MS. CURRY:</p> <p>14 Object to the form.</p> <p>15 A Perineal cornstarch with ovarian</p> <p>16 cancer?</p> <p>17 MS. THOMPSON:</p> <p>18 Q Correct. Let me phrase that</p> <p>19 differently just so it's clear.</p> <p>20 A Okay.</p> <p>21 Q Are you aware of any studies that link</p> <p>22 the perineal use of cornstarch products with</p> <p>23 ovarian cancer?</p> <p>24 MS. CURRY:</p>

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<p style="text-align: right;">Page 198</p> <p>1 Object to the form.</p> <p>2 A Therapeutically or just accidentally?</p> <p>3 MS. THOMPSON:</p> <p>4 Q Um -- as a substitute for talcum</p> <p>5 powder. If a woman is using corn -- a</p> <p>6 cornstarch-based perineal dusting powder, are you</p> <p>7 aware of any studies that have linked that usage</p> <p>8 to ovarian cancer?</p> <p>9 A Not that I -- no.</p> <p>10 Q Do you agree that -- I might go ahead</p> <p>11 and go back to that -- that -- the FDA, mark it</p> <p>12 as --</p> <p>13 A The letter?</p> <p>14 Q The letter.</p> <p>15 I know. But I don't have my stickers.</p> <p>16 MS. THOMPSON:</p> <p>17 My fault; not yours.</p> <p>18 THE COURT REPORTER:</p> <p>19 Okay.</p> <p>20 MS. THOMPSON:</p> <p>21 Shall we do another few just to get us</p> <p>22 to lunch?</p> <p>23 THE COURT REPORTER:</p> <p>24 I forget what number we're on.</p>	<p style="text-align: right;">Page 200</p> <p>1 summary on the following page, one, purpose and</p> <p>2 coverage of the final rule, and the last</p> <p>3 paragraph -- or the last sentence of the first</p> <p>4 paragraph says, "However, the use of powder on</p> <p>5 medical gloves presents numerous risks to</p> <p>6 patients and healthcare workers, including</p> <p>7 inflammation, granulomas and respiratory allergic</p> <p>8 reaction."</p> <p>9 Does that at least state what the FDA</p> <p>10 considers the reasons for the removal of talcum</p> <p>11 powder from surgical gloves?</p> <p>12 A Yes, it does.</p> <p>13 Q Are you aware that Health Canada</p> <p>14 determined that the migration of talc particles</p> <p>15 to the ovaries from perineal use was a plausible</p> <p>16 or is a plausible mechanism for the detection of</p> <p>17 talc in the ovaries?</p> <p>18 MS. CURRY:</p> <p>19 Object to the form.</p> <p>20 A I believe they did. You're --</p> <p>21 MS. THOMPSON:</p> <p>22 Q And you -- do you disagree with the</p> <p>23 determination that Health Canada reached</p> <p>24 regarding the -- the migration of talc particles</p>
<p style="text-align: right;">Page 199</p> <p>1 MS. THOMPSON:</p> <p>2 We're on --</p> <p>3 MS. EVERETT:</p> <p>4 14.</p> <p>5 MS. THOMPSON:</p> <p>6 14.</p> <p>7 (DEPOSITION NUMBER 14 WAS</p> <p>8 MARKED FOR IDENTIFICATION.)</p> <p>9 MS. THOMPSON:</p> <p>10 Q I'm going to go ahead and mark the FDA</p> <p>11 announcement on the banning of -- of talcum</p> <p>12 powder just so we can see what they actually did</p> <p>13 say about the reasons.</p> <p>14 And --</p> <p>15 A This is for gloves. For gloves.</p> <p>16 Surgical gloves.</p> <p>17 Q Examination and surgical gloves.</p> <p>18 A Yeah.</p> <p>19 Q And just in the bottom part of the</p> <p>20 right-hand side of the first page, "Banned</p> <p>21 Devices; Powdered Surgeon's Gloves, Powdered</p> <p>22 Patient Examination Gloves, and Absorbable Powder</p> <p>23 For Lubricating on a Surgeon's Glove."</p> <p>24 And if you'll turn to the executive</p>	<p style="text-align: right;">Page 201</p> <p>1 to the ovaries being a plausible mechanism for</p> <p>2 the detection of talc in ovaries?</p> <p>3 A Yes, I do.</p> <p>4 Q In your report, you state that the</p> <p>5 migration is contrary to basic anatomy and common</p> <p>6 sense, I believe.</p> <p>7 Do you still hold that opinion?</p> <p>8 A Where are you reading? Back to my</p> <p>9 report?</p> <p>10 Q I have to get your report out.</p> <p>11 A Yeah. That's get that out there.</p> <p>12 Q His expert report.</p> <p>13 And in the -- under "Migration" on page</p> <p>14 5, "Supposed Presence of Talc in Ovaries."</p> <p>15 A Ah. Okay. Yep.</p> <p>16 Q And Health Canada's conclusion was that</p> <p>17 the migration of talc particles to the ovaries</p> <p>18 from perineal use is a plausible mechanism for</p> <p>19 the detection of talc to the ovaries.</p> <p>20 But at least your opinion is that the</p> <p>21 presence of talc in the ovaries cannot be</p> <p>22 explained by migration. Is that right?</p> <p>23 A Well, the studies that I looked at here</p> <p>24 mostly are the presence of talc in cancer of the</p>

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<p style="text-align: right;">Page 202</p> <p>1 ovary, and there were some control patients, I</p> <p>2 believe, with breast cancer where they looked at</p> <p>3 the ovary.</p> <p>4 And these -- these studies have been</p> <p>5 around for a while. I've reviewed them multiple</p> <p>6 times, and they're just seriously flawed, from my</p> <p>7 perspective. So I don't know that you can</p> <p>8 conclude that. But these are -- these are just</p> <p>9 the studies that show the presence of talc in</p> <p>10 specimens. It's not the next line of evidence,</p> <p>11 which is actual variety of human -- human</p> <p>12 experiments, if you will, which are also</p> <p>13 seriously flawed.</p> <p>14 So, you know, I essentially reviewed</p> <p>15 all of that and came to the conclusion you can't</p> <p>16 conclude anything. There's no convincing data.</p> <p>17 Health Canada came to a different conclusion.</p> <p>18 Q And is that because Health Canada got</p> <p>19 it wrong again, or is that because scientists can</p> <p>20 come to different conclusions when reviewing the</p> <p>21 same data?</p> <p>22 MS. CURRY:</p> <p>23 Object to the form.</p> <p>24 A Based on my review on this, they got it</p>	<p style="text-align: right;">Page 204</p> <p>1 A I think they were mystified and they</p> <p>2 tried to argue that the reason why they found</p> <p>3 talc in everybody --</p> <p>4 MS. THOMPSON:</p> <p>5 Q Dr. Birrer, sorry.</p> <p>6 My question was: Do you know what the</p> <p>7 authors concluded?</p> <p>8 A I'm saying it.</p> <p>9 Q That's "yes" or "no."</p> <p>10 A Oh.</p> <p>11 Q Do you know what the authors concluded?</p> <p>12 MS. CURRY:</p> <p>13 Object to the form.</p> <p>14 A Yes.</p> <p>15 MS. THOMPSON:</p> <p>16 Q What did the authors conclude?</p> <p>17 A So I think they were mystified. And</p> <p>18 so --</p> <p>19 Q No. Did the authors -- where do you</p> <p>20 see in the paper that the authors were mystified?</p> <p>21 A Because --</p> <p>22 MS. CURRY:</p> <p>23 Let him finish and don't cut him off.</p> <p>24 MS. THOMPSON:</p>
<p style="text-align: right;">Page 203</p> <p>1 wrong.</p> <p>2 MS. THOMPSON:</p> <p>3 Q Regarding the Heller paper --</p> <p>4 A Uh-huh.</p> <p>5 Q -- let's just go back to your report.</p> <p>6 Do you know what the Heller authors</p> <p>7 concluded from their study?</p> <p>8 MS. CURRY:</p> <p>9 Object to the form.</p> <p>10 A Do you --</p> <p>11 MS. THOMPSON:</p> <p>12 Q This is the paper regarding the talc</p> <p>13 presence in --</p> <p>14 A Right.</p> <p>15 Q -- ovaries from the Heller paper.</p> <p>16 MS. CURRY:</p> <p>17 Object to the form.</p> <p>18 A So just to summarize real quick --</p> <p>19 MS. THOMPSON:</p> <p>20 Q No. Not asking that question.</p> <p>21 Do you know what the Heller authors</p> <p>22 concluded on the basis of their study?</p> <p>23 MS. CURRY:</p> <p>24 Object to the form.</p>	<p style="text-align: right;">Page 205</p> <p>1 Not when he's not answering my</p> <p>2 question.</p> <p>3 THE WITNESS:</p> <p>4 Well, I --</p> <p>5 MS. CURRY:</p> <p>6 He's trying to answer it. You keep</p> <p>7 cutting him off at every word.</p> <p>8 MS. THOMPSON:</p> <p>9 I asked where in the paper did the</p> <p>10 authors say they were mystified, and he needs to</p> <p>11 explain that.</p> <p>12 MS. CURRY:</p> <p>13 You haven't even marked the paper. You</p> <p>14 are asking him based on his expert report, and</p> <p>15 he's --</p> <p>16 MS. THOMPSON:</p> <p>17 I didn't ask him on the basis of his</p> <p>18 expert report. I asked him on the basis of his</p> <p>19 knowledge.</p> <p>20 I'll mark the Heller paper 15.</p> <p>21 (DEPOSITION EXHIBIT NUMBER 15 WAS</p> <p>22 MARKED FOR IDENTIFICATION.)</p> <p>23 MS. THOMPSON:</p> <p>24 Q Do you see anywhere in the paper that</p>

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<p style="text-align: right;">Page 206</p> <p>1 the authors were mystified? Yes or no?</p> <p>2 A I think they were confused by the lack</p> <p>3 of association.</p> <p>4 Q Do you see where the authors were</p> <p>5 mystified?</p> <p>6 MS. CURRY:</p> <p>7 Object to the form.</p> <p>8 MS. THOMPSON:</p> <p>9 Q There's nowhere where the authors say</p> <p>10 they were mystified, is there, Dr. Birrer?</p> <p>11 MS. CURRY:</p> <p>12 Object to the form.</p> <p>13 MS. THOMPSON:</p> <p>14 Q I'll withdraw the question.</p> <p>15 A Okay.</p> <p>16 Q Let's just go to the conclusions.</p> <p>17 "Conclusions: The detection of talc in</p> <p>18 all ovaries demonstrates that it can reach the</p> <p>19 upper genital tract."</p> <p>20 Is that what the authors of the Heller</p> <p>21 paper conclude?</p> <p>22 A Yes.</p> <p>23 Q And yet you're critical of the</p> <p>24 plaintiffs' experts because they conclude the</p>	<p style="text-align: right;">Page 208</p> <p>1 Q Is that your opinion?</p> <p>2 A Say that again.</p> <p>3 Q It's not that scientists can come to</p> <p>4 different conclusions. It's that the 12 experts</p> <p>5 who state the same conclusions as the authors of</p> <p>6 the paper are wrong and you're right?</p> <p>7 MS. CURRY:</p> <p>8 Object to the form.</p> <p>9 MS. THOMPSON:</p> <p>10 Q Is that a correct statement?</p> <p>11 A Correct.</p> <p>12 Q One of your criticisms of the Cramer</p> <p>13 paper from 2007 that detected talc in lymph nodes</p> <p>14 was that it was a case report; correct?</p> <p>15 A Correct.</p> <p>16 Q And you've published with Dr. Cramer;</p> <p>17 correct?</p> <p>18 A I don't think I'm on papers with</p> <p>19 Dr. Cramer.</p> <p>20 Q And have you seen the paper that was</p> <p>21 published recently of a series of cases in which</p> <p>22 talc was detected in the lymph nodes?</p> <p>23 MS. CURRY:</p> <p>24 Object to the form.</p>
<p style="text-align: right;">Page 207</p> <p>1 same thing that the authors of the paper</p> <p>2 conclude; right?</p> <p>3 MS. CURRY:</p> <p>4 Object to the form.</p> <p>5 MS. THOMPSON:</p> <p>6 Q In fact, I -- well, go ahead and</p> <p>7 answer.</p> <p>8 A Well, I'm critical of the paper and the</p> <p>9 experts who agreed with it.</p> <p>10 Q And I -- I think there were no fewer</p> <p>11 than 12 experts that you think were wrong on</p> <p>12 this; right?</p> <p>13 MS. CURRY:</p> <p>14 Object to the form.</p> <p>15 A If that's the number of experts that</p> <p>16 agreed to it, then, yeah. I agree on that.</p> <p>17 MS. THOMPSON:</p> <p>18 Q And it's not that scientists can come</p> <p>19 to different conclusions. It's that 12 experts</p> <p>20 who state the same conclusions as the authors of</p> <p>21 the paper are wrong and you're right?</p> <p>22 MS. CURRY:</p> <p>23 Object to the form.</p> <p>24 MS. THOMPSON:</p>	<p style="text-align: right;">Page 209</p> <p>1 A Do you have an author?</p> <p>2 MS. THOMPSON:</p> <p>3 Q Same authors.</p> <p>4 A So Dr. Cramer --</p> <p>5 Q The lead author is McDonald, but from</p> <p>6 Cramer's lab --</p> <p>7 A I have seen it.</p> <p>8 Q -- and Welch. You've seen it?</p> <p>9 A Uh-huh.</p> <p>10 Q And is it your understanding that the</p> <p>11 authors -- I'll mark the McDonald paper Exhibit</p> <p>12 16.</p> <p>13 (DEPOSITION EXHIBIT NUMBER 16 WAS</p> <p>14 MARKED FOR IDENTIFICATION.)</p> <p>15 MS. THOMPSON:</p> <p>16 Q Is it your understanding that the</p> <p>17 authors specifically controlled for any</p> <p>18 possibility of contamination?</p> <p>19 MS. CURRY:</p> <p>20 Object to the form.</p> <p>21 A No. That's not my understanding.</p> <p>22 MS. THOMPSON:</p> <p>23 Q Well, it's in the abstract, if we can</p> <p>24 get -- delve deeper if we need to. The authors</p>

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<p style="text-align: right;">Page 210</p> <p>1 said that since talc can be a surface contaminant</p> <p>2 from tissue collection preparation, digestion</p> <p>3 measurements may be influenced by contamination.</p> <p>4 Instead, because they preserve anatomic landmarks</p> <p>5 and permit identification of particles in cells</p> <p>6 and tissues polarized light microscopy and in</p> <p>7 situ SEM-EDX are recommended to assess talc in</p> <p>8 lymph nodes.</p> <p>9 And that's the methodology that the</p> <p>10 authors, the researchers, performed to assure</p> <p>11 themselves that this finding was not due to</p> <p>12 contamination; right?</p> <p>13 MS. CURRY:</p> <p>14 Object to the form.</p> <p>15 A You are reading correctly.</p> <p>16 MS. THOMPSON:</p> <p>17 Q I didn't even read that.</p> <p>18 A Oh.</p> <p>19 Q I came up with that --</p> <p>20 A Oh. I thought you were looking at the</p> <p>21 paper.</p> <p>22 Q Well, I must be right, then.</p> <p>23 A I mean, they -- they observe -- I read</p> <p>24 this -- I'll read it. "In conclusion, talc</p>	<p style="text-align: right;">Page 212</p> <p>1 MS. CURRY:</p> <p>2 Object to the form.</p> <p>3 A So they -- they observe -- they observe</p> <p>4 large amounts of contamination. They argue that</p> <p>5 with their technology, they can tell whether some</p> <p>6 is surface and some is internal, in lymph nodes.</p> <p>7 MS. THOMPSON:</p> <p>8 Q And they determined that some was</p> <p>9 internal; right?</p> <p>10 A I believe so.</p> <p>11 Q Probably have another, what, five</p> <p>12 minutes and then lunch, or I can do it after we</p> <p>13 come back.</p> <p>14 MS. CURRY:</p> <p>15 Is that okay with you?</p> <p>16 A That's okay.</p> <p>17 MS. CURRY:</p> <p>18 Is that okay with the court reporter?</p> <p>19 THE COURT REPORTER:</p> <p>20 That's fine. Yes.</p> <p>21 THE WITNESS:</p> <p>22 You all right? I'll stop mumbling.</p> <p>23 MS. THOMPSON:</p> <p>24 Q Okay. I want to go over just a few of</p>
<p style="text-align: right;">Page 211</p> <p>1 contamination in the surface of surgical</p> <p>2 pathology specimens of is common."</p> <p>3 Q Except -- and I didn't have a question</p> <p>4 on the table.</p> <p>5 A Okay.</p> <p>6 Q So I'll object to that as being</p> <p>7 nonresponsive to a question.</p> <p>8 Except the whole purpose of this study</p> <p>9 was to, number one, expand on the case report</p> <p>10 that was published earlier; right?</p> <p>11 MS. CURRY:</p> <p>12 Object to the form.</p> <p>13 A I don't see that. It's another study.</p> <p>14 MS. THOMPSON:</p> <p>15 Q Okay.</p> <p>16 A Yeah.</p> <p>17 Q But this had a series of 22 cases;</p> <p>18 right?</p> <p>19 A Twenty-two cases, correct.</p> <p>20 Q And -- and the authors concluded that</p> <p>21 by -- by using the techniques that they used in</p> <p>22 this pap- -- in this paper, they could confirm</p> <p>23 that the -- the talc in the lymph nodes was not</p> <p>24 surface contamination. Right?</p>	<p style="text-align: right;">Page 213</p> <p>1 your criticisms of plaintiffs' experts. And</p> <p>2 let's start with Dr. Clarke-Pearson. I believe</p> <p>3 that you have met Dr. Clarke-Pearson and know him</p> <p>4 by reputation, at least; correct?</p> <p>5 A I have.</p> <p>6 Q He's a past president, I believe, of</p> <p>7 SGO; correct?</p> <p>8 A Correct.</p> <p>9 Q And department chair at University of</p> <p>10 North Carolina, recently retired; correct?</p> <p>11 A Correct.</p> <p>12 Q And -- and you actually wrote the</p> <p>13 criticism here of Dr. Clarke-Pearson?</p> <p>14 A Correct.</p> <p>15 Q And that's your language?</p> <p>16 A Uh-huh.</p> <p>17 Q Okay. Let's just read through that.</p> <p>18 "Dr. Clarke-Pearson analogizes to the migration</p> <p>19 of sperm" -- and this is considering the</p> <p>20 migration of talc particles -- "into tubes after</p> <p>21 coitus. It is rather surprising to hear this</p> <p>22 from a gynecological oncologist."</p> <p>23 Did you look at Dr. Clarke-Pearson's</p> <p>24 references?</p>

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<p style="text-align: right;">Page 214</p> <p>1 A I looked at his expert report. 2 Q Including his references? 3 A I probably would have paged through it, 4 yeah. Yep. 5 Q "The obvious difficulty with this line 6 of reasoning is the fact that spermatozoa are 7 motile and have evolved under millions of years 8 to be able to migrate under their own control to 9 increase the potential to fertilize the egg. 10 This mode of transport is not consistent with a 11 talc particle." 12 Did you look at Dr. Pearson's citation 13 that describes the movement of dead sperm and 14 talc particles through that upper genital tract? 15 MS. CURRY: 16 Object to the form. 17 A Yeah. I didn't see the -- I didn't see 18 the reference on dead sperm. But -- 19 MS. THOMPSON: 20 Q If -- if there was a reference that 21 dead sperm moved through and moved through quite 22 easily, then your statement that it's not 23 analogous because spermatozoa are motile is 24 incorrect, isn't it?</p>	<p style="text-align: right;">Page 216</p> <p>1 A Are they dead dead or -- 2 Q Do you think dead sperm may be motile? 3 Do you know any -- too much about reproductive 4 physiology? 5 MS. CURRY: 6 Object to the form. 7 A A fair amount, yeah. 8 MS. THOMPSON: 9 Q And you don't know whether dead sperm 10 would be motile or not? 11 A So how are you defining that? 12 They're -- they're -- they've decayed? They're 13 broken down -- 14 Q Yes. 15 A -- or the flagella is not moving? 16 Q The flagella is not moving in a dead 17 sperm. 18 A Okay. 19 Q Is it? 20 A I guess as you are specifically 21 defining -- 22 Q Are you arguing me -- with me? 23 A Can I answer? 24 MS. CURRY:</p>
<p style="text-align: right;">Page 215</p> <p>1 MS. CURRY: 2 Object to the form. 3 A Well, I have to see the paper, and I 4 don't know the details. 5 MS. THOMPSON: 6 Q Assume with me that there is evidence 7 published in the peer-reviewed literature that 8 dead sperm and sperm particles move through the 9 upper genital tract, then your statement that 10 it's not analogous because spermatozoa are motile 11 would be incorrect; right? 12 MS. CURRY: 13 Object to the form. 14 A So these sperm would be put on the 15 perineum like a dusting? 16 MS. THOMPSON: 17 Q No. 18 A Okay. 19 Q I'm just saying it's -- your statement 20 that that is the reason would be incorrect. 21 A I -- so -- 22 Q Are -- are dead sperm motile? 23 A I don't actually know. They -- 24 Q You're --</p>	<p style="text-align: right;">Page 217</p> <p>1 I'm sorry. You can each just take 2 turns. Just please let her get her question out. 3 MS. THOMPSON: 4 Q Do you not know whether dead sperm 5 would be motile or not? 6 A I would think most of the time they 7 would not be motile. 8 Q Okay. And would you agree that a sperm 9 particle -- for example, if the flagellum is 10 broken off, would you agree that would not be 11 motile, a sperm particle? 12 MS. CURRY: 13 Object to the form. 14 A Motile, moving under its own -- 15 MS. THOMPSON: 16 Q Moving on its own. 17 A Yeah. I think it's unlikely. 18 Q Do you know the size of the head of a 19 sperm? 20 A No. 21 Q If the reason that Dr. Clarke-Pearson 22 was incorrect referencing dead and -- dead sperm 23 and sperm particles moving through the upper 24 genital tract could be relevant to a talc</p>

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<p style="text-align: right;">Page 218</p> <p>1 particle. If your reason for saying that opinion 2 is incorrect is that sperm are motile, then that 3 reasoning is incorrect, isn't it? 4 MS. CURRY: 5 Object to the form. 6 A Well, I think in the way it's expressed 7 here, that, obviously, it doesn't mean -- I mean, 8 it makes no sense to apply to spermatozoa, which 9 are mobile. But if you're telling me there's a 10 reference for dead sperm, then the question 11 becomes what's in that reference? So these -- 12 MS. THOMPSON: 13 Q Okay. 14 A -- dead sperm were deposited into the 15 uterus after coitus and -- 16 Q We're just talking -- we're not talking 17 about coitus. 18 Is it plausible to you -- 19 A Okay. 20 Q -- that a woman who has talcum on her 21 perineum -- 22 A Uh-huh. 23 Q -- could have coitus and the talcum 24 powder on the perineum could be placed in the</p>	<p style="text-align: right;">Page 220</p> <p>1 Object to the form. 2 A Yeah, I don't know what -- 3 MS. THOMPSON: 4 Q Those are your words. Are 5 Dr. Clarke-Pearson's opinions contrary to 6 knowledge of basic anatomy? 7 MS. CURRY: 8 Object to the form. 9 A Where are you reading? 10 MS. THOMPSON: 11 Q Well, for right now I was just in the 12 first paragraph of "Hypothesized migration of 13 talc to ovaries." 14 A What page? Is it on my report? 15 Q Page 7. 16 A Okay. 17 Oh. So you're relating that statement 18 to Clarke-Pearson? 19 Q Well, I believe you say that all the 20 experts have -- have a theory that's contrary to 21 basic anatomy and common sense. 22 A No. What that refers to, I think, is 23 the fact that you're putting -- you're dusting 24 the perineum many times, most of the times, in a</p>
<p style="text-align: right;">Page 219</p> <p>1 vagina forcefully? Is that plausible? 2 A I don't have any data on that. 3 Q Do you have to have data to say whether 4 or not that's plausible? 5 A I am a scientist. 6 Q Well, maybe take off your scientist 7 hat. Is it plausible that a woman who has talcum 8 powder on her perineum and has sex, that the 9 talcum powder could be forced into the vagina? 10 MS. CURRY: 11 Object to the form. 12 MS. THOMPSON: 13 Q Is it plausible? 14 A Sexual intercourse? 15 Q Sexual intercourse, yes. 16 A Yes. Just getting specifics. 17 Yeah. I mean, I -- I think the way 18 you're hypothesizing it, I suppose there's a 19 possibility. 20 Q So if those things are possible and 21 plausible, then you really don't think 22 Dr. Clarke-Pearson's opinions are unreasonable 23 and -- and are contrary to basic anatomy, do you? 24 MS. CURRY:</p>	<p style="text-align: right;">Page 221</p> <p>1 woman who's vertical, and this concept is that 2 somehow that talc and dust essentially ascends 3 into the ovary. And I think that more often than 4 not lacks common sense and basic anatomy because 5 of what I just said. 6 Now, if you want to go through each 7 individual study, I'm happy to do that because 8 there are methodologic flaws in them. But that 9 statement does not relate directly to 10 Dr. Clarke-Pearson. If it did, it would be under 11 his name. 12 Q But you talk generally about 13 plaintiffs' experts, too. And do you think that 14 you have a better understanding of female anatomy 15 than Dr. Clarke-Pearson? 16 MS. CURRY: 17 Object to the form. 18 A Dr. Clarke-Pearson's pretty good with 19 female anatomy. 20 MS. THOMPSON: 21 Q Do you think you have a better 22 understanding than Dr. Clarke-Pearson of female 23 reproductive physiology? 24 MS. CURRY:</p>

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<p style="text-align: right;">Page 222</p> <p>1 Object to the form.</p> <p>2 A No. I think he would be more versed in</p> <p>3 that.</p> <p>4 MS. THOMPSON:</p> <p>5 Q And -- and you've just testified that</p> <p>6 we're not just talking about a woman standing up</p> <p>7 and putting dusting powder and the ascension. We</p> <p>8 are talking about the possibility, in your words,</p> <p>9 that powder could be on the perineum and</p> <p>10 introduced in the vagina forcefully with sexual</p> <p>11 intercourse; right?</p> <p>12 A Well, yes --</p> <p>13 MS. CURRY:</p> <p>14 Object to the form.</p> <p>15 A We just had that conversation. I mean,</p> <p>16 again, it's hypothetical. Yeah.</p> <p>17 MS. THOMPSON:</p> <p>18 Q Okay. Agreed. I mean, I agree that's</p> <p>19 your opinion.</p> <p>20 And how about a woman who applies</p> <p>21 talcum powder to a sanitary napkin? Is it</p> <p>22 possible that the talcum powder would be</p> <p>23 introduced in the vagina through menstrual flow?</p> <p>24 A Through menstrual --</p>	<p style="text-align: right;">Page 224</p> <p>1 Q Do you think he would know it, what's</p> <p>2 published in literature?</p> <p>3 MS. CURRY:</p> <p>4 Object to the form.</p> <p>5 A He might.</p> <p>6 MS. THOMPSON:</p> <p>7 Q So you're certainly not opining today</p> <p>8 that you have a better understanding than</p> <p>9 Dr. Clarke-Pearson of materials that can travel</p> <p>10 retrograde through the upper genital tract, do</p> <p>11 you?</p> <p>12 MS. CURRY:</p> <p>13 Object to the form.</p> <p>14 A Oh, I disagree with that.</p> <p>15 MS. THOMPSON:</p> <p>16 Q You think you do have a better</p> <p>17 understanding than Dr. Clarke-Pearson regarding</p> <p>18 whether or not particles can travel through the</p> <p>19 upper genital tract?</p> <p>20 MS. CURRY:</p> <p>21 Object to the form.</p> <p>22 A Based upon my analysis of these papers,</p> <p>23 yes.</p> <p>24 MS. THOMPSON:</p>
<p style="text-align: right;">Page 223</p> <p>1 MS. CURRY:</p> <p>2 Object to the form.</p> <p>3 A Not that I know of. I don't have any</p> <p>4 data for that.</p> <p>5 MS. THOMPSON:</p> <p>6 Q Is that -- you don't think it's</p> <p>7 possible?</p> <p>8 A Again, from -- from -- it's</p> <p>9 interesting. So if menstrual flow coming out of</p> <p>10 the vagina with a sanitary napkin, the talc then</p> <p>11 gets into the vagina up to the ovaries. It</p> <p>12 doesn't make a lot of sense to me.</p> <p>13 Q What percentage of women have</p> <p>14 retrograde menstruation on a -- on a given</p> <p>15 period?</p> <p>16 A I don't understand what you mean by</p> <p>17 that.</p> <p>18 Q Do you think Dr. Clarke-Pearson</p> <p>19 probably knows that percentage?</p> <p>20 MS. CURRY:</p> <p>21 Object to the form.</p> <p>22 A I'm sure he'd probably have an opinion</p> <p>23 on it.</p> <p>24 MS. THOMPSON:</p>	<p style="text-align: right;">Page 225</p> <p>1 Q Well, you certainly didn't know about</p> <p>2 dead sperm and sperm particles, did you?</p> <p>3 MS. CURRY:</p> <p>4 Object to the form.</p> <p>5 A Well, it's one paper.</p> <p>6 MS. THOMPSON:</p> <p>7 Q And you don't know about -- you don't</p> <p>8 know how many -- what percentage of women have</p> <p>9 retrograde menstruation, which is a classic paper</p> <p>10 in gynecology -- gynecology? You don't know that</p> <p>11 percentage, do you?</p> <p>12 MS. CURRY:</p> <p>13 Object to the form.</p> <p>14 A I can't quote you that percentage.</p> <p>15 MS. THOMPSON:</p> <p>16 Q Do you know that women oftentimes use</p> <p>17 baby powder at bedtime?</p> <p>18 MS. CURRY:</p> <p>19 Object to the form.</p> <p>20 A I guess that's possible.</p> <p>21 MS. THOMPSON:</p> <p>22 Q And that would not be in an upright</p> <p>23 position, would it?</p> <p>24 MS. CURRY:</p>

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<p style="text-align: right;">Page 226</p> <p>1 Object to the form.</p> <p>2 A They may have put it on in an upright</p> <p>3 position.</p> <p>4 MS. THOMPSON:</p> <p>5 Q And do you agree that women could have</p> <p>6 powder on the perineum and use a tampon?</p> <p>7 MS. CURRY:</p> <p>8 Object to the form.</p> <p>9 A I assume that's possible, yes.</p> <p>10 MS. THOMPSON:</p> <p>11 Q And wouldn't it be possible that powder</p> <p>12 on a tampon could be introduced into the vagina?</p> <p>13 MS. CURRY:</p> <p>14 Object to the form.</p> <p>15 A It's possible.</p> <p>16 MS. THOMPSON:</p> <p>17 Q And what -- what did Dr. Kunz, K-U-N-Z,</p> <p>18 describe in an article regarding how particles</p> <p>19 and substances are transported to the upper</p> <p>20 genital tract?</p> <p>21 A So that's the peristaltic pump.</p> <p>22 Q And describe that for me.</p> <p>23 A Yeah. So they went and looked at the</p> <p>24 contractions -- they, first of all, tried to</p>	<p style="text-align: right;">Page 228</p> <p>1 Object to the form.</p> <p>2 A Yeah.</p> <p>3 The problem I have with that is I'm not</p> <p>4 sure what direction the pressure is in, because</p> <p>5 obviously if you give oxytocin at the time of</p> <p>6 pregnancy after the delivery, expels the</p> <p>7 placenta, so some of that pressure's going to</p> <p>8 come down.</p> <p>9 And, then, too, the radioactive studies</p> <p>10 are really problematic because a lot of times the</p> <p>11 label will come off of the microsphere. So you</p> <p>12 don't quite know where it's going.</p> <p>13 MS. THOMPSON:</p> <p>14 Q At what points in a female's -- in a</p> <p>15 woman's cycle are oxytocin levels the highest?</p> <p>16 A I can't quote you that.</p> <p>17 Q Would that be a question for</p> <p>18 Dr. Clarke-Pearson?</p> <p>19 MS. CURRY:</p> <p>20 Object to the form.</p> <p>21 A He probably would know.</p> <p>22 MS. THOMPSON:</p> <p>23 Q And are you aware of the studies</p> <p>24 showing that not only sperm particles and dead</p>
<p style="text-align: right;">Page 227</p> <p>1 measure the pressure in the uterus based on this</p> <p>2 contraction, and they used actually ultrasound to</p> <p>3 do it, which is an indirect measure, of course.</p> <p>4 Don't know really what the pressure is.</p> <p>5 Based upon finding that, then they went</p> <p>6 on to, if I recall correctly, use micro- --</p> <p>7 radiolabeled microspheres to do -- a word I can't</p> <p>8 pronounce -- hysterosalpingoscintigraphy,</p> <p>9 whatever.</p> <p>10 Q I can't either.</p> <p>11 A Yeah. And the idea was -- if I recall</p> <p>12 correctly, the idea of that whole study was</p> <p>13 actually for -- I think fertility and pregnancy.</p> <p>14 And the idea was that they then saw this</p> <p>15 radioactivity up in the areas and drew the</p> <p>16 conclusion that there is contraction to the</p> <p>17 uterus and that they were hypothesizing that the</p> <p>18 particles then were going up the tubes of the</p> <p>19 ovaries.</p> <p>20 Q So it facilitates movement through</p> <p>21 the --</p> <p>22 A Yeah.</p> <p>23 Q -- genital tract?</p> <p>24 MS. CURRY:</p>	<p style="text-align: right;">Page 229</p> <p>1 sperm move through the upper genital tract but</p> <p>2 even motile sperm move at a much faster rate than</p> <p>3 would be predicted strictly based on their</p> <p>4 self-generated motility?</p> <p>5 MS. CURRY:</p> <p>6 Object to the form.</p> <p>7 A Yeah. I actually recall seeing that in</p> <p>8 a study.</p> <p>9 MS. THOMPSON:</p> <p>10 Q Are you aware that motile sperm</p> <p>11 preferentially go to the side where ovulation has</p> <p>12 occurred?</p> <p>13 A That, I'm not -- I can't quote you</p> <p>14 that. I don't know.</p> <p>15 Q So that would probably be another</p> <p>16 question for one of the gynecologists or --</p> <p>17 MS. CURRY:</p> <p>18 Object to the form.</p> <p>19 MS. THOMPSON:</p> <p>20 Q -- gynecologic oncologists? Would you</p> <p>21 agree?</p> <p>22 A They -- they would have that, and their</p> <p>23 OB training would provide them with that</p> <p>24 information. Yeah.</p>

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<p style="text-align: right;">Page 230</p> <p>1 Q Let's break for lunch. 2 VIDEOGRAPHER: 3 Off the record at 12:55 p.m. 4 (Lunch recess.) 5 VIDEOGRAPHER: 6 We're back on the record at 2:02 p.m. 7 MS. THOMPSON: 8 Q Dr. Birrer, I think we established this 9 morning that it is your opinion that the genital 10 use of talcum powder is not a risk factor for 11 ovarian cancer; right? 12 A I'm sorry. Say that -- say that again. 13 Q It's your opinion that talcum powder is 14 not a risk factor for ovarian cancer; right? 15 A The use of talcum powder? 16 Q Yes. 17 A Correct. 18 Q Can you point me to any article -- can 19 you point me to an article that specifically 20 states genital talcum powder use is not a risk 21 factor for -- for ovarian cancer? 22 MS. CURRY: 23 Object to the form. 24 A That genital talcum powder use is not a</p>	<p style="text-align: right;">Page 232</p> <p>1 study? 2 MS. CURRY: 3 Object to the form. 4 A No. I'd have to go through them. Do 5 you have them? 6 MS. THOMPSON: 7 Q We're not gonna go through the 40 8 studies, but -- 9 At least sitting here today, you can't 10 think of one right offhand, can you? 11 A I'm happy to go through the studies. 12 Q Okay. Is it your opinion that genital 13 talcum powder use has been proven to be a safe 14 practice? 15 MS. CURRY: 16 Object to the form. 17 A We discussed that this morning. There 18 is no data I know that it's an unsafe practice. 19 That's a review of the literature. And, so, 20 it's -- I think in that context it's safe. 21 MS. THOMPSON: 22 Q In your previous -- or did you look at 23 websites when you prepared your report this time 24 regarding talcum powder exposure and the risk for</p>
<p style="text-align: right;">Page 231</p> <p>1 risk factor? I mean, if you look at the -- a lot 2 of the case-control studies, about 40 percent of 3 them are negative and -- 4 MS. THOMPSON: 5 Q Well -- and by negative, you mean not 6 statistically significant; right? 7 A (Nods affirmatively.) Negative. And 8 cohort studies aren't either. And -- and, 9 actually, that -- and the cohort studies have 10 been sort of analyzed, reanalyzed in multiple 11 meta-analysis, and so they're all negative. 12 Q But my question was: Did any of those 13 studies conclude talcum powder is not a risk 14 factor for ovarian cancer? 15 MS. CURRY: 16 Object to the form. 17 A So there are studies that don't show a 18 significant association between talcum use and -- 19 MS. THOMPSON: 20 Q But I'm looking for -- 21 A -- and ovarian cancer. 22 Q -- the statement that genital use of 23 talcum is not a risk factor for ovarian cancer. 24 Do you remember seeing that in any</p>	<p style="text-align: right;">Page 233</p> <p>1 ovarian cancer? 2 MS. CURRY: 3 Object to the form. 4 A Other than PubMed? 5 MS. THOMPSON: 6 Q Right. 7 Like the American Cancer Society or NCI 8 or any websites. 9 A Not for this one. 10 Q Had you looked at them before? 11 MS. CURRY: 12 Object to the form. 13 A I think in the previous depositions, I 14 reported looking at one or two of them. I'd have 15 to go back and look at that. 16 MS. THOMPSON: 17 Q Okay. 18 A Yeah. 19 Q And I think the American Cancer Society 20 website was one of those that you looked at. 21 Correct? 22 A Could be. 23 Q I'll mark 17, American Cancer Society, 24 Talcum Powder and Cancer.</p>

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<p style="text-align: right;">Page 234</p> <p>1 (DEPOSITION EXHIBIT NUMBER 17 2 WAS MARKED FOR IDENTIFICATION.) 3 MS. THOMPSON: 4 Q Does that look familiar? 5 A That looks like American Cancer 6 Society's website. Because I see the logo. 7 Q And -- and would you use this statement 8 on the American Cancer Society website to be 9 support for your opinion that talcum powder use 10 is not a risk factor for ovarian cancer? 11 A Is not a risk factor? Is not? 12 Q Is not. 13 A I wouldn't refer to this, no. 14 Q Do you think that's what this document 15 states? 16 A I don't think this -- it doesn't seem 17 to me, based on what the ACS is saying -- they 18 report that their findings are mixed, with some 19 studies reporting a slightly increased risk and 20 some reporting no increase. 21 Q So the American Cancer Society, on 22 their website, states that IARC has classified 23 talc that contains asbestos as carcinogenic to 24 humans; right?</p>	<p style="text-align: right;">Page 236</p> <p>1 talcum powder does not increase risk, are they? 2 MS. CURRY: 3 Object to the form. 4 A Say again. 5 MS. THOMPSON: 6 Q They're not saying that talcum powder 7 use does not increase cancer risk, do they? 8 A I don't see that stated. 9 Q And -- and they say there is some 10 suggestion of a possible increase in ovarian 11 cancer risk; right? 12 A Well, the statement I see is "It's not 13 clear if consumer products containing talcum 14 increase cancer risks." That's pretty specific. 15 Q They're saying it's not clear. It's 16 not saying it's not a risk, is it? 17 MS. CURRY: 18 Object to the form. 19 A They're saying they don't know. 20 MS. THOMPSON: 21 Q Right. And then the recommendation, by 22 the American Cancer Society, would be "Until more 23 information is available, people concerned about 24 using talcum powder may want to avoid or limit</p>
<p style="text-align: right;">Page 235</p> <p>1 A You're on page 3? 2 Q Yeah. 30 -- yeah, 3 of 6. 3 A Yeah. 4 Q And then based on the lack of data from 5 human studies and unlimited data in lab animal 6 studies, IARC classified inhaled talc not 7 containing asbestos as not classifiable; right? 8 A The second bullet? 9 Q The second bullet. 10 And then the third bullet is the IARC 11 that states that the perineal genital use of talc 12 powder -- talc-based body powder is possibly 13 carcinic- -- carcinogenic to humans. That's the 14 2B classification; right? 15 A 2B. 16 Q And then it states that the US National 17 Toxicology Program, NTB, has not fully reviewed 18 talc with or without asbestos as a possible 19 carcinogen; right? That's what it says. 20 A Correct. 21 Q And, then, as -- as you said, the ACS 22 states it's not clear if consumer products 23 containing talcum powder increase cancer risk. 24 They're certainly not saying that</p>	<p style="text-align: right;">Page 237</p> <p>1 their use of consumer products that contain it." 2 But you think any recommendation of 3 that kind is not indicated; correct? 4 MS. CURRY: 5 Object to the form. 6 A Well, it depends on how you read that. 7 I mean, I think what they're suggesting is that 8 people concerned about using talcum powder, for 9 whatever reason, may want to avoid or limit their 10 use of consumer products that contain it and 11 implies that it's the stress of knowing they're 12 using it because of what they've interpreted. It 13 doesn't really make any conclusions about talcum 14 powder. 15 MS. THOMPSON: 16 Q Are there any medical benefits that 17 you're aware of from the genital use of talcum 18 powder? 19 A Well, I think it's generally used to 20 absorb -- absorb fluid. It's -- a lot of women 21 like it. It's a body image issue. You know, so 22 I think those issues -- and again, I treat a lot 23 of women with ovarian cancer -- are important. 24 Q That wasn't my question.</p>

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<p style="text-align: right;">Page 238</p> <p>1 Are there any medical benefits to the</p> <p>2 genital use of talcum powder?</p> <p>3 MS. CURRY:</p> <p>4 Object to the form.</p> <p>5 A That is a medical use?</p> <p>6 MS. THOMPSON:</p> <p>7 Q Are there any benefits, is the</p> <p>8 question.</p> <p>9 A Yeah.</p> <p>10 MS. CURRY:</p> <p>11 Object to the form.</p> <p>12 MS. THOMPSON:</p> <p>13 Q Where are -- where are those benefits</p> <p>14 reported?</p> <p>15 A That's quality of life.</p> <p>16 Q Where in the medical literature can you</p> <p>17 show a report that describes medical benefits</p> <p>18 from the genital use of talcum powder?</p> <p>19 A Well, it's not in -- and again, I</p> <p>20 didn't review that for this expert report, so --</p> <p>21 but you're asking me.</p> <p>22 Q When you -- if you're trying to make a</p> <p>23 risk assessment, wouldn't you know if you're</p> <p>24 weighing the benefits versus the potential risks?</p>	<p style="text-align: right;">Page 240</p> <p>1 A Again, you asked me the question about</p> <p>2 do I think there's some medical benefit. I --</p> <p>3 the answer is yes. I mean --</p> <p>4 MS. THOMPSON:</p> <p>5 Q But that's never been published</p> <p>6 anywhere that you're aware of, has it?</p> <p>7 MS. CURRY:</p> <p>8 Object to the form.</p> <p>9 A As I said before, I -- I can't quote</p> <p>10 you that.</p> <p>11 MS. THOMPSON:</p> <p>12 Q Is it -- have you seen in the medical</p> <p>13 literature that there are no benefits, medical</p> <p>14 benefits from the use of talcum powder in the</p> <p>15 genital area?</p> <p>16 MS. CURRY:</p> <p>17 Object to the form.</p> <p>18 A I don't think I've actually seen that.</p> <p>19 MS. THOMPSON:</p> <p>20 Q Would you be surprised if there are</p> <p>21 references in numerous articles that say because</p> <p>22 there are no medical benefits of talcum powder</p> <p>23 use, it's not recommended?</p> <p>24 MS. CURRY:</p>
<p style="text-align: right;">Page 239</p> <p>1 A Well, I evaluated the risks, and there</p> <p>2 are none.</p> <p>3 Q So you just evaluated the risk and</p> <p>4 it -- it wouldn't matter to you whether there</p> <p>5 were benefits or not.</p> <p>6 A Well, my benefit --</p> <p>7 MS. CURRY:</p> <p>8 Object to the form.</p> <p>9 A I'm sorry. Go ahead. I'm sorry.</p> <p>10 Yeah. My benefit would be based upon</p> <p>11 my own experience. It's not necessarily</p> <p>12 published in medical literature.</p> <p>13 MS. THOMPSON:</p> <p>14 Q Okay. Well, that would certainly be</p> <p>15 anecdotal, wouldn't it?</p> <p>16 MS. CURRY:</p> <p>17 Object to the form.</p> <p>18 A Well, you know, I've got a lot of</p> <p>19 experience.</p> <p>20 MS. THOMPSON:</p> <p>21 Q It's still anecdotal, isn't it,</p> <p>22 Dr. Birrer?</p> <p>23 MS. CURRY:</p> <p>24 Object to the form.</p>	<p style="text-align: right;">Page 241</p> <p>1 Object to the form.</p> <p>2 A I'd be happy to -- I'd be happy to</p> <p>3 review them.</p> <p>4 MS. THOMPSON:</p> <p>5 Q Have you seen in the medical literature</p> <p>6 that cornstarch products are recommended if women</p> <p>7 choose to use a dusting powder over talcum</p> <p>8 powder?</p> <p>9 A Can you repeat that? I -- the cough.</p> <p>10 Q Have you seen in the medical literature</p> <p>11 that -- where cornstarch products are recommended</p> <p>12 if women choose to use a dusting powder over</p> <p>13 talcum powder?</p> <p>14 A You know, I haven't seen the -- I</p> <p>15 haven't seen the medical literature recommending</p> <p>16 cornstarch over talcum. But I have seen -- I've</p> <p>17 seen discussions about women who use cornstarch.</p> <p>18 Q And again, there have never been any</p> <p>19 risks that you're aware of into -- related to the</p> <p>20 genital use of cornstarch products and the link</p> <p>21 with ovarian cancer; right?</p> <p>22 A I don't know of any.</p> <p>23 Q You mentioned earlier this morning the</p> <p>24 National Academy of Science, Engineering and</p>

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<p>1 Medicine as a -- as a -- possibly the most</p> <p>2 reputable source of credible information.</p> <p>3 Would -- did I describe that sort of</p> <p>4 correctly?</p> <p>5 MS. CURRY:</p> <p>6 Object to the form.</p> <p>7 A I don't recall saying it's the most,</p> <p>8 but I used it in context of comparing IARC, if I</p> <p>9 recall correctly, versus some other sort of pure</p> <p>10 scientific professional organization, which I</p> <p>11 would include the National Academy to be that.</p> <p>12 MS. THOMPSON:</p> <p>13 Q Okay. Fair enough.</p> <p>14 And I'm sure you're familiar with the</p> <p>15 treatise -- it's actually -- came out in book</p> <p>16 form -- of the study by the Institute of</p> <p>17 Medicine, I believe, at that time, on ovarian</p> <p>18 cancer?</p> <p>19 A Yes.</p> <p>20 Q Did you participate at all in that</p> <p>21 study?</p> <p>22 A They asked me to review it.</p> <p>23 Q You were one of the reviewers?</p> <p>24 A They asked me to review it.</p>	<p>1 Q I'll give it to you in a minute.</p> <p>2 A Okay.</p> <p>3 Q I just want to ask you a few questions</p> <p>4 first.</p> <p>5 Why did you decline to review?</p> <p>6 A I was too busy.</p> <p>7 Q Okay. Because it was a big book?</p> <p>8 A It's monstrous.</p> <p>9 Q However, several of the authors have</p> <p>10 been coauthors with you on -- on papers. Is one</p> <p>11 of them Dr. Karlan?</p> <p>12 A I believe I've been on papers with</p> <p>13 Beth. And I think Anil Sood was on there, too.</p> <p>14 THE COURT REPORTER:</p> <p>15 Excuse me?</p> <p>16 THE WITNESS:</p> <p>17 Anil Sood, S-O-O-D.</p> <p>18 MS. THOMPSON:</p> <p>19 Q And Ronald Alvarez -- Alvarez published</p> <p>20 with you, I think?</p> <p>21 A I believe so.</p> <p>22 Q Dr. Karlan's published with you.</p> <p>23 A (Nods affirmatively.)</p> <p>24 Q Dr. Levine has published with you?</p>
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<p>1 Q Oh.</p> <p>2 A I declined.</p> <p>3 Q They asked you to review it and you did</p> <p>4 not review it. That explains it, because I</p> <p>5 didn't see your name on the list.</p> <p>6 And that was published in 2016?</p> <p>7 A Uh-huh.</p> <p>8 Q And what was your understanding of the</p> <p>9 purpose of that study?</p> <p>10 MS. CURRY:</p> <p>11 Object to the form.</p> <p>12 A It -- I -- you know, I think it was --</p> <p>13 this is -- it's just medicine undertakes this</p> <p>14 periodically for large topics, and that was one</p> <p>15 of them, to sort of summarize the state of the</p> <p>16 science.</p> <p>17 MS. THOMPSON:</p> <p>18 Q And the -- in fact, the committee that</p> <p>19 did the study was a committee on the state of the</p> <p>20 science in ovarian cancer research; is that</p> <p>21 correct? So you called --</p> <p>22 A This is the one by Beth Karlan?</p> <p>23 Q Yeah.</p> <p>24 A Yeah.</p>	<p>1 A Doug and I are on a couple of papers,</p> <p>2 yeah.</p> <p>3 Q Doug Levine?</p> <p>4 A Yeah.</p> <p>5 Q Dr. Odunsi, Kunle Odunsi --</p> <p>6 A Kunle. Kunle.</p> <p>7 Q -- has published with you. And</p> <p>8 Dr. Sood you mentioned; right?</p> <p>9 And Dr. -- is it Tworoger or --</p> <p>10 A Two- -- Twerger?</p> <p>11 Q -- Two- -- Twoauger?</p> <p>12 A T-W-O-G-G-E-R [sic].</p> <p>13 Q Has published with you?</p> <p>14 A I think so, yes. I'd have to check</p> <p>15 that.</p> <p>16 Q So you were, I would say, well</p> <p>17 represented on the --</p> <p>18 MS. CURRY:</p> <p>19 Object to the form.</p> <p>20 A Well, I know them.</p> <p>21 MS. THOMPSON:</p> <p>22 Q -- on the author list?</p> <p>23 MS. CURRY:</p> <p>24 Object to the form.</p>

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<p style="text-align: right;">Page 246</p> <p>1 MS. THOMPSON: 2 Q And -- and I assume you would agree 3 with me that the committee to report on the state 4 of the science of ovarian cancer research was 5 selected because of their expertise in the area; 6 correct? 7 A Yes. 8 MS. CURRY: 9 Object to the form. 10 MS. THOMPSON: 11 Q And, as we mentioned, this study was 12 under the auspices of the National Academy of 13 Science, Medicine and Engineering, Institute of 14 Medicine, I believe, originally; correct? 15 A Correct. 16 Q And is it your understanding that this 17 study was also supported by the CDC? 18 A That, I don't know. 19 Q All right. Let me just go ahead and 20 give it to you. 21 A Yeah. 22 (DEPOSITION EXHIBIT NUMBER 18 WAS 23 MARKED FOR IDENTIFICATION.) 24 MS. THOMPSON:</p>	<p style="text-align: right;">Page 248</p> <p>1 A Correct. 2 Q The State of the Science authors state, 3 under "Inflammation," "Studies of the 4 inflammatory marker C-reactive protein suggest a 5 possible association between inflammation and 6 increased risk of ovarian cancer," citing OC and 7 Poole. 8 "Other specific inflammatory factors 9 have also been associated with ovarian cancer." 10 Do you agree that the authors of this 11 treatise reported that there's a possible 12 association between inflammation and increased 13 risk for ovarian cancer? 14 A Well, on these -- on these two 15 sentences, I think they accurately stated, 16 "suggests association." And then they refer -- I 17 don't -- these two papers, I can't directly quote 18 you. I mean -- 19 Q And I -- and I'm not -- 20 A Yeah. 21 Q -- suggesting that they do anything 22 other than suggest the possible association. 23 A Right. 24 Q I'm not trying to read more into it.</p>
<p style="text-align: right;">Page 247</p> <p>1 Q Exhibit 18 I'm marking as Ovarian 2 Cancers, Evolving Paradigms in Research and Care. 3 And this is not the entire book, but it is the 4 entire chapter that we're going to look at, which 5 is "Prevention and Early Detection," Chapter 3. 6 And if you look on page little ix, page 7 9, preface -- 8 A 9? 9? 9 Q Little nine. 10 A Yeah. 11 Q Yeah. The -- the first sentence, "This 12 congressionally mandated report sponsored by the 13 Centers For Disease Control and Prevention 14 assesses the state of research on ovarian cancers 15 from multiple perspectives and by multiple 16 disciplines." 17 So do you agree that the Center For 18 Disease Control sponsored the study? 19 A Correct. 20 Q If you'll turn to page -- I don't have 21 pages on my copy. Page 110. Under the section 22 heading "Inflammation." And this is in a larger 23 section titled "Behavioral and Inflammatory Risk 24 Factors"; correct?</p>	<p style="text-align: right;">Page 249</p> <p>1 A Okay. 2 Q And then they describe "A meta-analysis 3 reported that exposure to asbestos was associated 4 with a 77 percent increased risk of ovarian 5 cancer mortality," citing Carmargo. 6 Are you familiar with that paper? 7 A I am familiar with that. That's the 8 occasional exposure, if I recall correctly. 9 Q And "The International Agency For 10 Research on Cancer determined that there was 11 sufficient evidence to support a causal 12 relationship between asbestos exposure and 13 ovarian cancer." 14 So the authors of this treatise include 15 exposure to asbestos and its association with 16 ovarian cancer in the Inflammation section of -- 17 of risk factors; right? 18 A Say that again? Sorry. For asbestos? 19 Q The authors of this treatise include 20 exposure to asbestos and its association with 21 ovarian cancer in the Inflammation section of 22 risk factors; right? 23 A Correct. 24 Q They go on to say, "This has led to</p>

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<p>1 studies of talc use which is chemically similar</p> <p>2 to asbestos and can cause an inflammatory</p> <p>3 response."</p> <p>4 Do you agree with that statement?</p> <p>5 A I -- I actually hesitate a little on</p> <p>6 that because I'm not so sure that that's a</p> <p>7 temporal relationship, that it was the asbestos</p> <p>8 association that then led to the investigation of</p> <p>9 talc. I don't know, when Dan Cramer published</p> <p>10 his first paper, that's what was driving him.</p> <p>11 Q Do you have any other disagreement with</p> <p>12 the -- the statement other than whether it led to</p> <p>13 the studies of talc use?</p> <p>14 MS. CURRY:</p> <p>15 Object to the form.</p> <p>16 A I don't know. Again, we've covered</p> <p>17 this. I'm not a mineralogist, so I don't know</p> <p>18 the similarity issues. And inflammatory response</p> <p>19 is not defined. So other than that, it's fine.</p> <p>20 MS. THOMPSON:</p> <p>21 Q Well, the authors -- let's take out the</p> <p>22 asbestos and say "Talc can cause inflammatory</p> <p>23 response." Do you agree or disagree with that?</p> <p>24 A Well, inflammation is a broad issue and</p>	<p>1 one else anywhere in the literature to question</p> <p>2 even this, I don't agree with.</p> <p>3 MS. THOMPSON:</p> <p>4 Q Okay. So you -- so you disagree with</p> <p>5 the authors including that statement in -- in</p> <p>6 this treatise?</p> <p>7 A I just think it's not defined. They</p> <p>8 defined it, then I would have felt a lot better.</p> <p>9 Can cause granulomas inflammatory response. That</p> <p>10 would have been more accurate.</p> <p>11 Q I can understand that you think it</p> <p>12 should have been defined better.</p> <p>13 A Yeah.</p> <p>14 Q But do you agree with the statement</p> <p>15 that's in this treatise, or disagree?</p> <p>16 MS. CURRY:</p> <p>17 Object to the form.</p> <p>18 A No opinion.</p> <p>19 MS. THOMPSON:</p> <p>20 Q But you'll agree that at least these</p> <p>21 experts thought it was worthwhile putting the</p> <p>22 statement in this State of the Science treatise</p> <p>23 on ovarian cancer published in 2016; right?</p> <p>24 MS. CURRY:</p>
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<p>1 it's very relevant to this debate, which is are</p> <p>2 we talking granulomas, acute, chronic but</p> <p>3 nongranuloma? I think that's a big issue.</p> <p>4 Q Well, these were the authors that were</p> <p>5 selected because of their expertise to do a State</p> <p>6 of the Science treatise at the behest of the</p> <p>7 National Academy of Science and CDC.</p> <p>8 I'm just asking you do you agree with</p> <p>9 the statement "Talc can cause an inflammatory</p> <p>10 response"?</p> <p>11 MS. CURRY:</p> <p>12 Object to the form.</p> <p>13 A And -- and I'm -- I'm answering it.</p> <p>14 MS. THOMPSON:</p> <p>15 Q And you say you don't know? You can't</p> <p>16 agree or disagree? Is that what you're saying?</p> <p>17 MS. CURRY:</p> <p>18 Object to the form.</p> <p>19 A The inflammation is not defined. I</p> <p>20 don't know if the similarity between asbestos and</p> <p>21 talc. So other than that, I think it's fine.</p> <p>22 But the -- the -- the implication that all of the</p> <p>23 ovarian cancer experts are on this -- on this --</p> <p>24 on this report and there are no one -- there's no</p>	<p>1 Object to the form.</p> <p>2 A Yeah. Apparently.</p> <p>3 MS. THOMPSON:</p> <p>4 Q Do you know Jason Wright?</p> <p>5 A Division head at Columbia?</p> <p>6 Q Yes.</p> <p>7 A I do know Jason. Not -- I know him by</p> <p>8 reputation. I don't think I've ever actually met</p> <p>9 him.</p> <p>10 Q And what is his reputation?</p> <p>11 A I think he's got a good reputation</p> <p>12 running his division, and he's a good surgeon.</p> <p>13 Q Have you ever published with Jason</p> <p>14 Wright?</p> <p>15 A I don't believe so.</p> <p>16 Q You're right. That was a trick</p> <p>17 question.</p> <p>18 I'm gonna mark --</p> <p>19 MS. CURRY:</p> <p>20 I should have objected.</p> <p>21 (DEPOSITION EXHIBIT NUMBER 19</p> <p>22 WAS MARKED FOR IDENTIFICATION.)</p> <p>23 MS. THOMPSON:</p> <p>24 I'm gonna mark just a short article of</p>

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<p>1 Jason Wright's as Exhibit Number 19.</p> <p>2 Sorry. I thought I gave you mine.</p> <p>3 THE WITNESS:</p> <p>4 We're done with IM?</p> <p>5 MS. THOMPSON:</p> <p>6 Q Yeah, I think so. And this was an</p> <p>7 article published in -- not an article. It's</p> <p>8 a -- under a practice issue, which I think is an</p> <p>9 ongoing column, basically, in The Green Journal.</p> <p>10 What's The Green Journal?</p> <p>11 A OB-GYN, I think?</p> <p>12 Q And is that the journal that -- the</p> <p>13 journal that's published under the ACOG auspices?</p> <p>14 A I believe so.</p> <p>15 Q Are you a member of ACOG?</p> <p>16 A No.</p> <p>17 Q And this was published in December of</p> <p>18 2018, about six months ago. And was titled "Best</p> <p>19 Articles From the Past Year." And the second</p> <p>20 article listed out of four -- and these were</p> <p>21 what's new in ovarian cancer -- is the</p> <p>22 Penninkilampi article published in Epidemiology.</p> <p>23 A Uh-huh.</p> <p>24 Q And Dr. Wright concludes that, bottom</p>	<p>1 THE WITNESS:</p> <p>2 Oh, leaving you in the dust? Sorry.</p> <p>3 And then the use -- UKC talc studies,</p> <p>4 it really pales in comparison because -- and I</p> <p>5 looked at Penninkilampi pretty carefully. It</p> <p>6 kind of revisited all of the previous data. I</p> <p>7 think -- I -- I would assume that Jason doesn't</p> <p>8 necessarily keep up with this literature, so when</p> <p>9 it came out, he looked at it and said, ah, it's a</p> <p>10 meta-analysis. But it doesn't bring much to the</p> <p>11 table, I think.</p> <p>12 MS. THOMPSON:</p> <p>13 Q Well, you're obviously speculating as</p> <p>14 to Dr. Wright's reasoning, because neither --</p> <p>15 neither one of us knows. But at least Dr. Wright</p> <p>16 chose to include this as one of the four best</p> <p>17 articles regarding ovarian cancer in the past</p> <p>18 year published in 2018; right?</p> <p>19 MS. CURRY:</p> <p>20 Object to the form.</p> <p>21 A Well, I think he -- I think he -- I</p> <p>22 think he exposed his reasoning a little bit by</p> <p>23 the last sentence in the first paragraph. "The</p> <p>24 possible association with talcum and brain cancer</p>
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<p>1 line, "Perineal application of talc is associated</p> <p>2 with a small increased risk of ovarian cancer."</p> <p>3 Do you disagree with that conclusion by</p> <p>4 Dr. Wright?</p> <p>5 MS. CURRY:</p> <p>6 Object to the form.</p> <p>7 A That's his -- I'm trying to figure out</p> <p>8 where you're reading. It's the bottom-line</p> <p>9 statement?</p> <p>10 MS. THOMPSON:</p> <p>11 Q Bottom line, yes.</p> <p>12 A Yeah, I would disagree with that.</p> <p>13 Q Do you disagree with it -- the</p> <p>14 inclusion of the Penninkilampi meta-analysis as</p> <p>15 one of the best articles from the past year?</p> <p>16 MS. CURRY:</p> <p>17 Object to the form.</p> <p>18 A You know, it's interesting. I would,</p> <p>19 actually. I -- when -- when you compare it to</p> <p>20 Aerial Three and the Carbon Inhibitors and the</p> <p>21 hypothermic intraperineal chemotherapy, which was</p> <p>22 a New England Journal paper --</p> <p>23 MS. THOMPSON:</p> <p>24 Can you slow down?</p>	<p>1 has attracted media attention, resulting in a</p> <p>2 number of lawsuits."</p> <p>3 So I think that's part of the reason he</p> <p>4 feels this is relevant. Doesn't bring a lot of</p> <p>5 science.</p> <p>6 MS. THOMPSON:</p> <p>7 Q Well, I don't think it was meant to</p> <p>8 bring science. He was choosing this article for</p> <p>9 its -- its relevance for the readership of the</p> <p>10 American College of OB-GYN journal; correct?</p> <p>11 MS. CURRY:</p> <p>12 Object to the form.</p> <p>13 A I would agree with that.</p> <p>14 MS. THOMPSON:</p> <p>15 Q Do you have an opinion as to whether</p> <p>16 talc, the mineral talc, is inert?</p> <p>17 MS. CURRY:</p> <p>18 Object to the form.</p> <p>19 A You have to define "inert."</p> <p>20 MS. THOMPSON:</p> <p>21 Q Do you have an opinion as to whether</p> <p>22 the mineral talc, if it occurs in pure form --</p> <p>23 I'll add that as well -- is chemically inert?</p> <p>24 MS. CURRY:</p>

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<p style="text-align: right;">Page 258</p> <p>1 Object to the form.</p> <p>2 A Chemically inert, meaning -- again, I'm</p> <p>3 struggling with this, that it -- it -- it can</p> <p>4 enter into chemical reaction with other</p> <p>5 substances.</p> <p>6 MS. THOMPSON:</p> <p>7 Q I'd just seen that phrase used, so I</p> <p>8 wanted to see if you had an understanding of what</p> <p>9 it meant and -- and whether it's -- that</p> <p>10 statement would be true.</p> <p>11 A I really would need -- if -- if you've</p> <p>12 seen it said, do you have it so I can look at it?</p> <p>13 Q I've seen it by your -- your fellow</p> <p>14 experts.</p> <p>15 A And -- and what was the context? There</p> <p>16 must have been a context.</p> <p>17 Q And the context was talc is chemically</p> <p>18 inert. Would you have an opinion on that?</p> <p>19 MS. CURRY:</p> <p>20 Object to the form.</p> <p>21 A I think I would say no opinion right</p> <p>22 now.</p> <p>23 MS. THOMPSON:</p> <p>24 Q Okay. Is it biologically inert?</p>	<p style="text-align: right;">Page 260</p> <p>1 MS. CURRY:</p> <p>2 Sorry.</p> <p>3 A That, I don't think I could say with</p> <p>4 confidence.</p> <p>5 MS. THOMPSON:</p> <p>6 Q So even though talc used for</p> <p>7 pleurodesis is biologically -- is not</p> <p>8 biologically inert, you wouldn't be able to say</p> <p>9 whether baby powder was or not?</p> <p>10 A Well, we --</p> <p>11 MS. CURRY:</p> <p>12 Object to the form.</p> <p>13 A Well, we didn't put baby powder into</p> <p>14 the pleural cavities of patients, so we really</p> <p>15 haven't done that.</p> <p>16 MS. THOMPSON:</p> <p>17 Q Would you have any reason to suspect</p> <p>18 that baby powder would behave in a less</p> <p>19 biologically active manner than the talc used in</p> <p>20 pleurodesis?</p> <p>21 MS. CURRY:</p> <p>22 Object to the form.</p> <p>23 A Well, the talc -- you know, the talc</p> <p>24 used in pleurodesis is -- and I'm putting</p>
<p style="text-align: right;">Page 259</p> <p>1 MS. CURRY:</p> <p>2 Object to the form.</p> <p>3 MS. THOMPSON:</p> <p>4 Q Pure mineral talc. If pure talc</p> <p>5 existed.</p> <p>6 MS. CURRY:</p> <p>7 Object to the form.</p> <p>8 A Huh?</p> <p>9 Okay.</p> <p>10 That's another difficult one. I mean,</p> <p>11 I think that we know talc is used for</p> <p>12 pleurodesis. So that's -- is that a biologic</p> <p>13 process? I think it probably would qualify. So</p> <p>14 I wouldn't call it inert from that standpoint.</p> <p>15 MS. THOMPSON:</p> <p>16 Q And you're not gonna get me to argue</p> <p>17 with that.</p> <p>18 A I don't think so.</p> <p>19 Q Would that opinion apply to Johnson's</p> <p>20 baby powder?</p> <p>21 MS. CURRY:</p> <p>22 Object to the form.</p> <p>23 MS. THOMPSON:</p> <p>24 Q Or do you know?</p>	<p style="text-align: right;">Page 261</p> <p>1 quotations around this -- relatively pure, and</p> <p>2 it's gonna be different than the baby powder.</p> <p>3 But if you're asking me is talc in baby powder, I</p> <p>4 think we can agree on that. And, so, by analogy,</p> <p>5 I would expect some biologic activity.</p> <p>6 MS. THOMPSON:</p> <p>7 Q Okay.</p> <p>8 A Okay.</p> <p>9 Q And same for Shower to Shower?</p> <p>10 MS. CURRY:</p> <p>11 Object to the form.</p> <p>12 A Actually don't even know -- I've never</p> <p>13 seen a Shower to Shower container, but it's the</p> <p>14 product; right?</p> <p>15 MS. THOMPSON:</p> <p>16 Q Do you know what's in Shower to Shower?</p> <p>17 A I'm assuming it's analogous to baby</p> <p>18 powder.</p> <p>19 Q If -- well, would -- would that opinion</p> <p>20 apply to fibrous talc?</p> <p>21 MS. CURRY:</p> <p>22 Object to the form.</p> <p>23 A You know, again, I'm not a mineralogy</p> <p>24 expert, so I'm not going to make a comment on</p>

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<p style="text-align: right;">Page 262</p> <p>1 that.</p> <p>2 MS. THOMPSON:</p> <p>3 Q Do you know what fibrous talc is?</p> <p>4 A I'm not sure I can really define it.</p> <p>5 Q And it's your understanding that</p> <p>6 fibrous talc or talc with asbestiform fibers is</p> <p>7 specifically excluded from the IARC 2010</p> <p>8 monograph? Correct?</p> <p>9 A Say that again, please.</p> <p>10 Q Is it your -- let me rephrase it just a</p> <p>11 little bit. Is it your understanding that</p> <p>12 fibrous talc or talc with asbestiform fibers is</p> <p>13 specifically excluded from the IARC 2010</p> <p>14 monograph?</p> <p>15 MS. CURRY:</p> <p>16 Object to the form.</p> <p>17 A So that's -- asbestiform fibers or</p> <p>18 asbestos?</p> <p>19 MS. THOMPSON:</p> <p>20 Q Asbestiform fibers. Is there a</p> <p>21 difference between fibrous talc and talc with</p> <p>22 asbestiform fibers?</p> <p>23 MS. CURRY:</p> <p>24 Object to the form.</p>	<p style="text-align: right;">Page 264</p> <p>1 A It sounds like it, yes. Habit. It's a</p> <p>2 different definition of habit than I'm used to.</p> <p>3 MS. THOMPSON:</p> <p>4 Q And I think you probably recall when we</p> <p>5 were discussing Health Canada, they were also</p> <p>6 referring to talc, nonasbestiform talc; right?</p> <p>7 MS. CURRY:</p> <p>8 Object to the form.</p> <p>9 A I believe so.</p> <p>10 MS. THOMPSON:</p> <p>11 Q And in the -- let's go ahead and mark</p> <p>12 the 2012 IARC that relates to asbestos.</p> <p>13 (DEPOSITION EXHIBIT NUMBER 20</p> <p>14 WAS MARKED FOR IDENTIFICATION.)</p> <p>15 MS. THOMPSON:</p> <p>16 Q That'd be Exhibit 20. And on the first</p> <p>17 page, 219, "The conclusions" -- reading in the</p> <p>18 first paragraph -- "The conclusions reached in</p> <p>19 this monograph about asbestos and its</p> <p>20 carcinogenic risk apply to these six type of</p> <p>21 fibers wherever they are found, and that includes</p> <p>22 talc-containing asbestiform fibers."</p> <p>23 A Yes.</p> <p>24 Q Is that your understanding of this?</p>
<p style="text-align: right;">Page 263</p> <p>1 A Again, I -- I -- that's not in my area</p> <p>2 of expertise.</p> <p>3 MS. THOMPSON:</p> <p>4 Q So you don't know --</p> <p>5 A No.</p> <p>6 Q -- whether there's any difference or</p> <p>7 not?</p> <p>8 A I have no opinion.</p> <p>9 Q And -- well, we can look at the 2010 --</p> <p>10 A Uh-huh.</p> <p>11 Q -- monograph to -- to clarify that.</p> <p>12 So on page 277 --</p> <p>13 A Uh-huh.</p> <p>14 Q -- "Talc may also form" -- reading in</p> <p>15 paragraph 3 --</p> <p>16 A Uh-huh.</p> <p>17 Q -- "Talc may also form as true mineral</p> <p>18 fibers that are asbestiform. Asbestiform</p> <p>19 describes the pattern of growth of a mineral that</p> <p>20 is referred to as a habit."</p> <p>21 And you would agree that that is not</p> <p>22 the same as talc with asbestos; right?</p> <p>23 MS. CURRY:</p> <p>24 Object to the form.</p>	<p style="text-align: right;">Page 265</p> <p>1 A I see that. Yeah.</p> <p>2 MS. CURRY:</p> <p>3 Object to the form.</p> <p>4 MS. THOMPSON:</p> <p>5 Q Would your opinions regarding the</p> <p>6 biological activity of baby powder apply as well</p> <p>7 to baby powder that contains asbestos?</p> <p>8 MS. CURRY:</p> <p>9 Object to the form.</p> <p>10 A Not asbestiform but asbestos?</p> <p>11 MS. THOMPSON:</p> <p>12 Q Asbestiform, it -- talc with asbestos</p> <p>13 is talc with asbestos.</p> <p>14 A Okay.</p> <p>15 Q Talc with --</p> <p>16 A So it wouldn't change -- it wouldn't</p> <p>17 change my view.</p> <p>18 Q Okay. And what about baby powder that</p> <p>19 contains heavy metals like chromium, nickle, and</p> <p>20 cobalt?</p> <p>21 MS. CURRY:</p> <p>22 Object to the form.</p> <p>23 A No.</p> <p>24 MS. THOMPSON:</p>

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<p>1 Q And what about baby powder with</p> <p>2 chemicals that are either possible or known</p> <p>3 carcinogens, like styrene, coumarin, eugenol,</p> <p>4 D'Limonine, p-Cresol, muscutone or benzophenone.</p> <p>5 MS. CURRY:</p> <p>6 Object to the form.</p> <p>7 MS. THOMPSON:</p> <p>8 Q Would it change your opinion regarding</p> <p>9 the biologic activity of baby powder?</p> <p>10 A Well, looking at the biologic activity</p> <p>11 of baby powder, based upon what I reviewed, the</p> <p>12 answer is no because it doesn't matter what's in</p> <p>13 that. We looked at the biologic activity.</p> <p>14 Q So it doesn't matter to you whether</p> <p>15 there are known carcinogens in baby powder?</p> <p>16 MS. CURRY:</p> <p>17 Object to the form.</p> <p>18 A Well, based upon the studies, then we</p> <p>19 would have seen convincing evidence of biologic</p> <p>20 causality. We didn't.</p> <p>21 MS. THOMPSON:</p> <p>22 Q And you're referring to the</p> <p>23 epidemiology studies?</p> <p>24 MS. CURRY:</p>	<p>1 A Okay. Okay. Thank you.</p> <p>2 (DEPOSITION EXHIBIT NUMBER 21 WAS</p> <p>3 MARKED FOR IDENTIFICATION.)</p> <p>4 MS. THOMPSON:</p> <p>5 Q This is Exhibit 21, "Asbestos Exposure</p> <p>6 and Ovarian Fiber Burden."</p> <p>7 Have you seen this paper, Dr. Birrer?</p> <p>8 A So I don't think -- let me -- I don't</p> <p>9 think I reviewed this. Let me just check.</p> <p>10 Well, it was on my list. I must have.</p> <p>11 Q And again, just going to the</p> <p>12 conclusions of these authors, the last paragraph</p> <p>13 in the abstract.</p> <p>14 A Uh-huh.</p> <p>15 Q "This study demonstrates that asbestos</p> <p>16 can reach the ovary. Although the number of</p> <p>17 subjects is small, asbestos appears to be present</p> <p>18 in ovarian tissue more frequently and in higher</p> <p>19 amounts in women with a documentable exposure</p> <p>20 history."</p> <p>21 Do you agree that was the conclusion of</p> <p>22 the authors?</p> <p>23 A That's what they state.</p> <p>24 Q And on page 438, last paragraph, "The</p>
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<p>1 Object to the form.</p> <p>2 A I'm referring to all of it.</p> <p>3 MS. THOMPSON:</p> <p>4 Q Would the presence of known carcinogens</p> <p>5 provide a plausible mechanism?</p> <p>6 MS. CURRY:</p> <p>7 Object to the form.</p> <p>8 A Mechanisms for -- for what?</p> <p>9 MS. THOMPSON:</p> <p>10 Q For possible carcinogenesis.</p> <p>11 MS. CURRY:</p> <p>12 Object to the form.</p> <p>13 A But we didn't see carcinogenesis.</p> <p>14 There's no plausible biologic association or --</p> <p>15 so I'm not sure what we're designing a mechanism</p> <p>16 for.</p> <p>17 MS. THOMPSON:</p> <p>18 Q And are you familiar with the Heller</p> <p>19 paper regarding the finding of asbestos in human</p> <p>20 ovaries?</p> <p>21 A The Heller paper --</p> <p>22 Q 1996?</p> <p>23 A The one we just reviewed or --</p> <p>24 Q I'm handing you a new one.</p>	<p>1 fact that exposure to a husband is more</p> <p>2 significant than exposure to a father suggests a</p> <p>3 possible role for sexual contact as the</p> <p>4 transporting vector for asbestos fibers."</p> <p>5 Would you agree that if sexual -- if</p> <p>6 sexual contact was a transporting vector, that</p> <p>7 the fibers would enter the peritoneal cavity and</p> <p>8 ovaries through the vagina?</p> <p>9 MS. CURRY:</p> <p>10 Object to the form.</p> <p>11 A Just ask that once more, please.</p> <p>12 MS. THOMPSON:</p> <p>13 Q That wasn't a very good question. The</p> <p>14 problem is I don't know exactly how to make it</p> <p>15 better.</p> <p>16 If -- if the authors are proposing</p> <p>17 sexual contact as a possible means for</p> <p>18 transporting the asbestos fibers into -- into the</p> <p>19 ovaries, would -- wouldn't you assume that that</p> <p>20 would be via a vaginal route?</p> <p>21 A Yeah, I wouldn't assume that. I think</p> <p>22 one of the challenges here is that there are more</p> <p>23 differences between a wife and a daughter than</p> <p>24 just sexual activity. Wives may be in close</p>

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<p>1 contact with their husband in terms of --</p> <p>2 Q But that's not the question I'm asking.</p> <p>3 I'm saying if sexual contact is a</p> <p>4 transporting vector, wouldn't you assume that</p> <p>5 that would be through a vaginal route, not</p> <p>6 inhalation or some other way?</p> <p>7 MS. CURRY:</p> <p>8 Object to the form.</p> <p>9 A If -- if sexual activity was the</p> <p>10 mechanism of transport, is that what you're</p> <p>11 saying?</p> <p>12 MS. THOMPSON:</p> <p>13 Q Right.</p> <p>14 A Yeah.</p> <p>15 It's kind of a non sequitur. I mean,</p> <p>16 you're making the assumption sexual contact, and</p> <p>17 then you're asking, well, if that's it -- if</p> <p>18 that's the mode of transmission, is that the mode</p> <p>19 of transmission. Well, then, you've already</p> <p>20 assumed it, so -- so I could --</p> <p>21 Q Okay. I just wanted to make sure</p> <p>22 you're assuming it because the authors don't</p> <p>23 specifically say, you know, the -- the asbestos</p> <p>24 comes from a perineal exposure --</p>	<p>1 Correct?</p> <p>2 A So it's household contact with men who</p> <p>3 had fairly high exposure. So I think you can</p> <p>4 probably assume it was a substantial amount of</p> <p>5 exposure.</p> <p>6 Q What's your basis for assuming that</p> <p>7 it's a substantial amount of exposure?</p> <p>8 A Well, these men, if they're working in</p> <p>9 the asbestos area, are going to be covered with</p> <p>10 it. That's been shown, which is unfortunate,</p> <p>11 but, yeah.</p> <p>12 Q Can you point me to any study that</p> <p>13 compares how much exposure there would be in a</p> <p>14 talc mine versus a woman using talcum powder on</p> <p>15 her perineum daily or twice daily for -- for</p> <p>16 decades?</p> <p>17 MS. CURRY:</p> <p>18 Object to the form.</p> <p>19 A Well, this is not talc. This is not</p> <p>20 talc; this is asbestos.</p> <p>21 MS. THOMPSON:</p> <p>22 Q I know. That's a separate question.</p> <p>23 It's not in the article.</p> <p>24 A Okay. Can you ask that again?</p>
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<p>1 A Well, they're making -- yeah. They're</p> <p>2 making that distinction between a daughter and --</p> <p>3 Q Yeah, they are. I just wanted to make</p> <p>4 sure we are understanding that.</p> <p>5 And in the conclusions, "In our study,</p> <p>6 the women with a positive exposure history had</p> <p>7 asbestos detected in their ovaries more</p> <p>8 frequently and in higher counts."</p> <p>9 If that did indeed happen, that would</p> <p>10 argue against any kind of laboratory</p> <p>11 contamination, wouldn't it?</p> <p>12 MS. CURRY:</p> <p>13 Object to the form.</p> <p>14 A I'm just checking the numbers. I'm</p> <p>15 sorry.</p> <p>16 9 of 13 household, 6 of 17 and about</p> <p>17 one out of -- one out of 17.</p> <p>18 So, you know, I think -- I think it's</p> <p>19 fair to say that laboratory contamination should</p> <p>20 be more equal in all groups. It doesn't</p> <p>21 completely eliminate it, but...</p> <p>22 MS. THOMPSON:</p> <p>23 Q And these were exposed through</p> <p>24 household contact, not occupational exposure.</p>	<p>1 Q Can you point me to any study that</p> <p>2 compares how much exposure there would be in a</p> <p>3 talc mine versus a woman using talcum powder on</p> <p>4 her perineum daily or twice daily for decades?</p> <p>5 MS. CURRY:</p> <p>6 Object to the form.</p> <p>7 A Yeah. I don't think that's been asked</p> <p>8 and qualified. So it's difficult.</p> <p>9 MS. THOMPSON:</p> <p>10 Q Is the fact that asbestos causes</p> <p>11 pleural and peritoneal mesothelioma relevant to</p> <p>12 whether or not talcum powder can cause ovarian</p> <p>13 cancer?</p> <p>14 MS. CURRY:</p> <p>15 Object to the form.</p> <p>16 A Not to the data that I -- and the</p> <p>17 studies that I reviewed.</p> <p>18 MS. THOMPSON:</p> <p>19 Q And I don't think this was clear to me</p> <p>20 this morning.</p> <p>21 How does asbestos get to the</p> <p>22 peritoneum, in your opinion?</p> <p>23 MS. CURRY:</p> <p>24 Object to the form.</p>

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<p style="text-align: right;">Page 274</p> <p>1 MS. THOMPSON: 2 Q Or do you not know? 3 A Well, I -- I summarized my 4 understanding as not being necessarily an 5 asbestos expert, but my clinical experience, 6 which is asbestos, obviously, is a risk factor 7 for mesothelioma and for lung cancer. If it's 8 inhaled, then it's -- it's transiting to the 9 pleural cavity, which is where, then, it's 10 inducing mesothelioma. 11 And then there are peritoneal 12 mesotheliomas. And I don't honestly think we 13 know precisely how it gets there. There is -- 14 there is some evidence that pleural activities 15 can communicate with peritoneal activities. And 16 the example I'd give you on that is if one has 17 malignant ascites, fluid in the peritoneal 18 cavity, it frequently ends up in the pleural 19 cavities. 20 So -- so -- but you've got diaphragm 21 there with parietal pleura covering it. So 22 exactly how that happens, I don't know. 23 Q Is migration or transport through the 24 genital tract of asbestos a plausible mechanism</p>	<p style="text-align: right;">Page 276</p> <p>1 women who are massively exposed? 2 A I think that's the epidemiologic data 3 I'm aware of. 4 Q You're not aware of the epidemiology 5 that includes household or domestic exposure? 6 MS. CURRY: 7 Object to the form. 8 A Secondary exposures? 9 MS. THOMPSON: 10 Q Correct. 11 A Yeah. Yeah. I know that. I know that 12 a little bit less than the initial occupational 13 exposure. Most -- most of that came from the 14 Army. 15 Q And you'll agree that you don't have 16 any literature that compares what that exposure 17 would be compared to an exposure with someone 18 using talcum powder on their genitals for -- 19 A I agree. 20 Q -- for an extended period of time? 21 A Yes. 22 Q So I want to understand. You don't 23 know whether asbestos fibers can migrate or be 24 transported up the genital tract, but you're</p>
<p style="text-align: right;">Page 275</p> <p>1 for asbestos getting into the peritoneal cavity? 2 MS. CURRY: 3 Object to the form. 4 A Yeah, I don't -- I don't know the 5 answer to that. The increased incidence of 6 ovarian cancer in asbestos-exposed women, I mean, 7 I think it's -- it's agreed upon that those women 8 had massive exposures. So -- 9 MS. THOMPSON: 10 Q What -- what's your basis for saying 11 those women had massive exposures? 12 A Well, my impression is that in gas mask 13 manufacturing -- 14 And, of course, this is in the second 15 world war. 16 -- there wasn't really an appreciation 17 how bad asbestos is. And, so, they got exposed 18 to certainly levels that, you know, average 19 people would not. And even -- even in towns that 20 had cement factories and issues like that, those 21 studies were really not all that positive. But 22 the gas masks are. 23 Q Is it your opinion that the studies 24 that link asbestos with ovarian cancer are all in</p>	<p style="text-align: right;">Page 277</p> <p>1 confident that talc cannot. Is that right? 2 MS. CURRY: 3 Object to the form. 4 A Well, that's part of the reason I don't 5 think asbestos -- we can't say that. If I 6 remember, the question was can -- can the genital 7 tract be an explanation for the asbestos fibers. 8 In my opinion, no, we don't know that. And the 9 data we have from talc suggests, no, that doesn't 10 happen. 11 MS. THOMPSON: 12 Q Still not clear. 13 So asbestos, you don't know; but talc, 14 you know it doesn't. Is that right? 15 MS. CURRY: 16 Object to the form. 17 A Well, I would say, you know, if you -- 18 if you want to pursue that, then I would say, 19 based upon the talc data, which has actually been 20 examined, that it's unlikely that asbestos is 21 going up through the genital tract. 22 MS. THOMPSON: 23 Q So, in your opinion, that is not a 24 plausible mechanism for asbestos reaching the</p>

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<p style="text-align: right;">Page 278</p> <p>1 ovaries?</p> <p>2 A Correct.</p> <p>3 Q And what is your explanation for</p> <p>4 household members of asbestos working -- workers</p> <p>5 having an increased risk of ovarian cancer and</p> <p>6 mesothelioma?</p> <p>7 MS. CURRY:</p> <p>8 Object to the form.</p> <p>9 A Well, again, not being an asbestos</p> <p>10 expert, but I would assume this is inhalation,</p> <p>11 much like other exposures to asbestos, and then</p> <p>12 absorption through the lung parenchyma and</p> <p>13 ultimately through this pleural perineal process.</p> <p>14 MS. THOMPSON:</p> <p>15 Q But it's your opinion that the transfer</p> <p>16 or migration of the fibers through coitus is not</p> <p>17 plausible?</p> <p>18 MS. CURRY:</p> <p>19 Object to the form.</p> <p>20 A I don't know the data for that.</p> <p>21 MS. THOMPSON:</p> <p>22 Q Well, you don't know data for the other</p> <p>23 routes either, do you?</p> <p>24 MS. CURRY:</p>	<p style="text-align: right;">Page 280</p> <p>1 lot more data for -- if it's something to do with</p> <p>2 genital transport than you do for other -- other</p> <p>3 methods, but --</p> <p>4 A Well, I am a scientist.</p> <p>5 MS. CURRY:</p> <p>6 Object to the form.</p> <p>7 MS. THOMPSON:</p> <p>8 Q Well, it's selective science.</p> <p>9 MS. CURRY:</p> <p>10 Object to the form and argumentative.</p> <p>11 MS. THOMPSON:</p> <p>12 Q If you are advising a patient, could</p> <p>13 you reassure her that talcum powder containing</p> <p>14 asbestos is safe to use on the perineum?</p> <p>15 A It's -- it's an irrelevant issue.</p> <p>16 Q Okay. Patient says, Dr. Birrer, is it</p> <p>17 safe for me to continue using baby powder on the</p> <p>18 per- -- on my perineum. And your answer would</p> <p>19 be?</p> <p>20 A Yes.</p> <p>21 Q And if -- assuming that baby powder</p> <p>22 is -- is shown to contain asbestos, would your</p> <p>23 advice be the same?</p> <p>24 MS. CURRY:</p>
<p style="text-align: right;">Page 279</p> <p>1 Object to the form.</p> <p>2 A Well, there's a lot of literature for,</p> <p>3 you know, shipyard builders where they got</p> <p>4 exposed to asbestos. They get both pleural and</p> <p>5 perineal mesothelioma.</p> <p>6 MS. THOMPSON:</p> <p>7 Q We're talking about household exposure.</p> <p>8 A But again, that's data to tell us,</p> <p>9 under the extreme conditions, where and how that</p> <p>10 might migrate.</p> <p>11 Q Well, but you don't believe Heller, who</p> <p>12 proposed that sexual transmission was a plausible</p> <p>13 route for -- for the asbestos fibers in contacts</p> <p>14 to have a higher incidence of ovarian cancer in</p> <p>15 perineal mesothelioma; right?</p> <p>16 MS. CURRY:</p> <p>17 Object to the form.</p> <p>18 A Well, they didn't say that. They</p> <p>19 didn't say that. They said it's possible.</p> <p>20 MS. THOMPSON:</p> <p>21 Q Okay.</p> <p>22 A They're proposing a hypothesis and I</p> <p>23 said, well, show me the data.</p> <p>24 Q Okay. Well, it seems like you need a</p>	<p style="text-align: right;">Page 281</p> <p>1 Object to the form.</p> <p>2 MS. THOMPSON:</p> <p>3 Q Would your answer be the same?</p> <p>4 A So this is a hypothetical?</p> <p>5 Q Yeah.</p> <p>6 A Powder is the -- is -- is then</p> <p>7 determined to have asbestos?</p> <p>8 Q Correct.</p> <p>9 A Again, so is the question am I</p> <p>10 recommending a patient use asbestos?</p> <p>11 Q Yeah. That's the question.</p> <p>12 A Yeah. No, I wouldn't do that.</p> <p>13 Q Did you read Dr. Longo's report?</p> <p>14 A You know, that came up.</p> <p>15 Can you -- do you have a copy of it to</p> <p>16 refresh my memory?</p> <p>17 Q I do.</p> <p>18 (DEPOSITION EXHIBIT NUMBER 22 WAS</p> <p>19 MARKED FOR IDENTIFICATION.)</p> <p>20 MS. THOMPSON:</p> <p>21 Q I'm gonna mark -- Exhibit 22 is</p> <p>22 Dr. Longo's report in the MDL.</p> <p>23 Exhibit 23 is Dr. Longo's supplemental</p> <p>24 report in the MDL.</p>

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<p>1 (DEPOSITION EXHIBIT NUMBER 23 WAS 2 MARKED FOR IDENTIFICATION.) 3 MS. THOMPSON: 4 Q Do you remember seeing these reports? 5 MS. CURRY: 6 Do you have an extra copy? 7 MS. THOMPSON: 8 I do. 9 MS. CURRY: 10 Thank you. 11 A It's not on my list. 12 MS. THOMPSON: 13 Q Did you ask to see any testing on 14 Johnson's baby powder to see if it contained 15 asbestos? 16 A No, I did not. I think I came across 17 this, actually, previously, but not in this one. 18 Q And understanding that you're -- well, 19 I assume that you're not an expert in asbestos 20 testing; right? 21 A Correct. 22 Q Assuming that -- and if you want to 23 read the report, we can go off the record. 24 But assuming that Dr. Longo found</p>	<p>1 telling a patient it was safe to use baby powder 2 on her genitals if it contained -- if two-thirds 3 of the bottles contained asbestos? 4 MS. CURRY: 5 Object to the form. 6 A You know, again, I'm gonna emphasize 7 this. My review of the data suggests that -- 8 that those products are not a risk for ovarian 9 cancer. 10 MS. THOMPSON: 11 Q I -- I'm clear -- 12 A Regardless of what the hypothetical is. 13 Q I'm clear on that. 14 A Okay. 15 Q But -- but this is not really even a 16 hypothetical. This is testing that has shown 17 two-thirds of the baby powder samples contain 18 asbestos. 19 Do -- would you still feel good about 20 advising a patient that it's safe? 21 MS. CURRY: 22 Object to the form. 23 A I would -- I would tell them that based 24 on my review of the literature, extensive review</p>
Page 283	Page 285
<p>1 between 60 and 70 percent of bottles, historical 2 samples provided by Johnson & Johnson over 3 decades to contain asbestos, would that impact 4 how you would advise a patient who says, 5 Dr. Birrer, is it safe for me to use Johnson's 6 baby powder on my perineum? 7 MS. CURRY: 8 Object to the form. 9 A So, again, this -- this gets to the 10 point of having reviewed all the literature in 11 terms of the product, Shower to Shower, 12 Johnson & Johnson's baby powder, as increasing 13 the risk for ovarian cancer showing biological 14 plausibility. 15 Careful review of that literature has 16 shown nothing. So whether there's asbestos in 17 there or not, I don't know. 18 MS. THOMPSON: 19 Q Would -- would it give you pause? 20 MS. CURRY: 21 Object to the form. 22 A Pause. I don't know what pause is. 23 MS. THOMPSON: 24 Q Would you have some concern about</p>	<p>1 of the literature, it is a safe product. 2 MS. THOMPSON: 3 Q And what if they said, Dr. Birrer, is 4 that true even if it does contain asbestos? 5 MS. CURRY: 6 Object to the form. 7 MS. THOMPSON: 8 Q Would your answer be the same? 9 A I would -- I would -- you know, I would 10 say, again, it doesn't matter if that's the way 11 the product was used. And it was careful 12 studies. 13 Q Have you seen any studies from 14 Johnson & Johnson regarding their asbestos 15 testing? 16 A I haven't seen that. 17 Q Were you shown any testing results from 18 Johnson & Johnson? 19 A No. 20 Q Were you shown any testing results from 21 defense experts as to whether baby powder 22 contained asbestos? 23 MS. CURRY: 24 Object to the form.</p>

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<p style="text-align: right;">Page 286</p> <p>1 A Not that I recall, although, as I said</p> <p>2 before, in the expert witness reports, the ones</p> <p>3 that involved minerals in asbestos, I went</p> <p>4 through them fairly rapidly.</p> <p>5 MS. THOMPSON:</p> <p>6 Q Do you know if any defense experts even</p> <p>7 performed any testing as to whether there was</p> <p>8 asbestos in baby powder?</p> <p>9 A No.</p> <p>10 Q Do you know -- did you see that</p> <p>11 Dr. Longo also tested for talc fibers, so-called</p> <p>12 fibrous talc?</p> <p>13 MS. CURRY:</p> <p>14 Object to the form.</p> <p>15 A Fibrous talc. I can't quote you that,</p> <p>16 but I'll rely on you.</p> <p>17 MS. THOMPSON:</p> <p>18 Q Dr. Longo found -- and, you know, feel</p> <p>19 free to look to that summary -- virtually every</p> <p>20 Johnson's baby powder and Shower to Shower sample</p> <p>21 provided from historical samples contained talc</p> <p>22 fibers. The same answer as to asbestos; it</p> <p>23 doesn't matter?</p> <p>24 MS. CURRY:</p>	<p style="text-align: right;">Page 288</p> <p>1 A No, I didn't. I see the litigation ad.</p> <p>2 MS. THOMPSON:</p> <p>3 Q Okay. I'm gonna give you -- I'm gonna</p> <p>4 mark as Exhibit 24 a report -- call it an article</p> <p>5 because it's titled "News" -- from BMJ. And</p> <p>6 what's BMJ?</p> <p>7 A I don't know. I was gonna ask you.</p> <p>8 Q Oh. British Medical Journal. You've</p> <p>9 heard of the British Medical Journal?</p> <p>10 A Yes. I thought it was Birmingham.</p> <p>11 Q I -- that was another trick question.</p> <p>12 I said it was a news report from a medical</p> <p>13 journal.</p> <p>14 And you can take a minute to look</p> <p>15 through that --</p> <p>16 A Please.</p> <p>17 Q -- since you haven't seen the news</p> <p>18 reports.</p> <p>19 So you'll, I think, agree with me that</p> <p>20 the editors didn't come to any conclusions as to</p> <p>21 whether or not baby powder caused ovarian cancer;</p> <p>22 right?</p> <p>23 A Correct.</p> <p>24 Q But they -- the editors of the journal</p>
<p style="text-align: right;">Page 287</p> <p>1 Object to the form.</p> <p>2 A There again, these products that he's</p> <p>3 analyzing have been used for years. We have the</p> <p>4 epi data. It's unconvincing. We've got the</p> <p>5 biologic data. It's definitely unconvincing.</p> <p>6 The inflammatory theory is inconsistent. So to</p> <p>7 say anything other than that this is a safe</p> <p>8 product, I think, is inappropriate.</p> <p>9 MS. THOMPSON:</p> <p>10 Q Are -- are you aware of news reports</p> <p>11 over the past two or three months of the presence</p> <p>12 of asbestos in baby powder and</p> <p>13 Johnson & Johnson's knowledge of the asbestos in</p> <p>14 baby powder?</p> <p>15 MS. CURRY:</p> <p>16 Object to the form.</p> <p>17 A I'm not.</p> <p>18 (DEPOSITION EXHIBIT NUMBER 24</p> <p>19 WAS MARKED FOR IDENTIFICATION.)</p> <p>20 MS. THOMPSON:</p> <p>21 Q You haven't seen any news reports about</p> <p>22 asbestos in baby powder?</p> <p>23 MS. CURRY:</p> <p>24 Object to the form.</p>	<p style="text-align: right;">Page 289</p> <p>1 at least thought it important to -- to report the</p> <p>2 claims that baby powder may contain asbestos;</p> <p>3 correct?</p> <p>4 MS. CURRY:</p> <p>5 Object to the form.</p> <p>6 A I think they thought this would be of</p> <p>7 interest to the readership.</p> <p>8 MS. THOMPSON:</p> <p>9 Q Agreed.</p> <p>10 And you don't think the editors would</p> <p>11 have published this news report if it wasn't</p> <p>12 based on what they considered credible evidence,</p> <p>13 would you?</p> <p>14 MS. CURRY:</p> <p>15 Object to the form.</p> <p>16 A I would -- I would not agree with that</p> <p>17 statement. I think they would -- they might not</p> <p>18 agree with any of this or the role of talcum</p> <p>19 powder or asbestos, but -- but they felt their</p> <p>20 readership would be interested in this.</p> <p>21 MS. THOMPSON:</p> <p>22 Q So BMJ has become the National Enquirer</p> <p>23 of medical journals now?</p> <p>24 MS. CURRY:</p>

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<p>1 Object to the form.</p> <p>2 A Medical journals are not above some</p> <p>3 editorial latitude.</p> <p>4 MS. THOMPSON:</p> <p>5 Q And why would the readers be</p> <p>6 interested?</p> <p>7 MS. CURRY:</p> <p>8 Object to the form.</p> <p>9 A Well, I think there -- there is major</p> <p>10 litigation involved. There are a number of court</p> <p>11 cases. The FDA has weighed in a little bit. And</p> <p>12 then there are, quote, internal documents. All</p> <p>13 of that is, for lack of a better word, you know,</p> <p>14 scientists are looking for things to excite their</p> <p>15 lives, so this is entertainment.</p> <p>16 MS. THOMPSON:</p> <p>17 Q Might it be that BMJ thought their</p> <p>18 doctors would want to tell patients about this</p> <p>19 information?</p> <p>20 MS. CURRY:</p> <p>21 Object to the form.</p> <p>22 MR. MIZGALA:</p> <p>23 So now you're --</p> <p>24 MS. THOMPSON:</p>	<p>1 conclusions. You're a physician and you see this</p> <p>2 article. Might it be something that you would be</p> <p>3 interested in so you could advise your patients</p> <p>4 accordingly?</p> <p>5 MS. CURRY:</p> <p>6 Object to the form.</p> <p>7 A Definitely not.</p> <p>8 MS. THOMPSON:</p> <p>9 Q And you would not give a medical</p> <p>10 journal any credit that doctors might want to</p> <p>11 advise their patients that baby powder contains</p> <p>12 asbestos?</p> <p>13 MS. CURRY:</p> <p>14 Object to the form.</p> <p>15 A I think they do a reasonable job of</p> <p>16 simply reporting what is happening. And they</p> <p>17 talk about -- they talk about internal documents.</p> <p>18 Those are essentially impossible to assess. They</p> <p>19 talk about the New York Times. Not a scientific</p> <p>20 organization. There is some hearsay from the</p> <p>21 FDA. And then they -- they out line the court</p> <p>22 case. I wouldn't -- I would not take this and</p> <p>23 translate it into some recommendation for a</p> <p>24 patient.</p>
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<p>1 Q Just a hunch. Just a hunch.</p> <p>2 MR. MIZGALA:</p> <p>3 Now you're asking him to speculate.</p> <p>4 You've been doing this the whole deposition.</p> <p>5 MS. GARBER:</p> <p>6 I don't think we're doing speaking</p> <p>7 objections. So the objection is to form.</p> <p>8 MR. MIZGALA:</p> <p>9 Yeah. But she's gone to task for</p> <p>10 speculating earlier, and she's doing the same</p> <p>11 thing.</p> <p>12 MS. GARBER:</p> <p>13 Okay. The objection is to form. You</p> <p>14 know that. Let's follow the rules.</p> <p>15 A Say again.</p> <p>16 MS. THOMPSON:</p> <p>17 Q You're a physician that reads journals.</p> <p>18 A Uh-huh.</p> <p>19 Q As a physician, let's -- we're going to</p> <p>20 take a hypothetical that you're not involved in</p> <p>21 talcum powder litigation. Okay?</p> <p>22 A Uh-huh.</p> <p>23 Q And you haven't done this thorough</p> <p>24 review that you have done to come to your</p>	<p>1 MS. THOMPSON:</p> <p>2 Q So it wouldn't be any different from</p> <p>3 reading a story about the Kardashians in BMJ?</p> <p>4 MS. CURRY:</p> <p>5 Object to the form.</p> <p>6 MS. THOMPSON:</p> <p>7 Q Is that what you're saying?</p> <p>8 A You want an answer to that?</p> <p>9 Q Sure. It was a question.</p> <p>10 A Yeah, it's different.</p> <p>11 Q Okay. Thanks.</p> <p>12 A It's about talc.</p> <p>13 Q Are you aware that concerns have been</p> <p>14 raised about the safety of pleurodesis?</p> <p>15 MS. CURRY:</p> <p>16 Object to the form.</p> <p>17 A So, actually, my understanding of</p> <p>18 pleurodesis, at least in the relationship of talc</p> <p>19 in ovarian cancer, there's essentially no</p> <p>20 evidence linking the two. But let me -- let me</p> <p>21 see what you're referring to.</p> <p>22 MS. THOMPSON:</p> <p>23 Q Well, I was just -- let me ask</p> <p>24 questions first.</p>

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<p>1 A Uh-huh.</p> <p>2 Q And that was: Are you aware that</p> <p>3 concerns have been raised about the safety of</p> <p>4 pleurodesis?</p> <p>5 MS. CURRY:</p> <p>6 Object to the form.</p> <p>7 A No.</p> <p>8 MS. THOMPSON:</p> <p>9 Q And have you been -- are you aware --</p> <p>10 no, you're not aware of any concerns at all.</p> <p>11 Let me go ahead and give you Exhibit</p> <p>12 25.</p> <p>13 (DEPOSITION EXHIBIT NUMBER 25</p> <p>14 WAS MARKED FOR IDENTIFICATION.)</p> <p>15 MS. THOMPSON:</p> <p>16 Q And this is a letter to the editor.</p> <p>17 I --</p> <p>18 A Uh-huh.</p> <p>19 Q -- I understand that. It's not a</p> <p>20 formal study, per se.</p> <p>21 MS. CURRY:</p> <p>22 Do you have an extra copy?</p> <p>23 MS. THOMPSON:</p> <p>24 Yeah, I do.</p>	<p>1 stating that talc is asbestos-free should not</p> <p>2 release us from a responsibility to the patient,</p> <p>3 especially when safe alternatives are available."</p> <p>4 And the picture is of a talc fiber</p> <p>5 found in a pleurodesis talc.</p> <p>6 Does that cause you any concern?</p> <p>7 MS. CURRY:</p> <p>8 Object to the form.</p> <p>9 A It doesn't. To be fair, the entire --</p> <p>10 my -- my impression is, although I don't do -- I</p> <p>11 do pleurodesis for cancer patients, in which</p> <p>12 case, unfortunately, longevity makes this whole</p> <p>13 issue moot. But we've moved away from talc for</p> <p>14 other reasons. It's painful. It doesn't work</p> <p>15 all the time. We have better agents. So that</p> <p>16 kind of makes this moot.</p> <p>17 But, you know, again I think you</p> <p>18 pointed out appropriately. It's -- they're</p> <p>19 entitled to their opinions. It's a single</p> <p>20 article -- it's a single letter, and the studies</p> <p>21 addressing this are very limited. So I think --</p> <p>22 I think they're -- making fairly bold statements</p> <p>23 on not a lot of data.</p> <p>24 MS. THOMPSON:</p>
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<p>1 Q Do you know Dr. -- I think it's Ghio.</p> <p>2 I don't know how it's pronounced. Do you know</p> <p>3 Ghio and Dr. Roggli?</p> <p>4 A I don't know either of them.</p> <p>5 Q And I'll let you read through this.</p> <p>6 Let's just read that -- I'm gonna read the last</p> <p>7 paragraph and get your thoughts.</p> <p>8 A Okay.</p> <p>9 Q "The assertion that contemporary</p> <p>10 purified preparations of talc do not contain</p> <p>11 asbestos, therefore eliminating a risk of</p> <p>12 mesothelioma, should be closely examined prior to</p> <p>13 its acceptance for clinical application. The</p> <p>14 methodology used to confirm the lack of</p> <p>15 asbestiform materials in a finished product,</p> <p>16 (i.e., X-ray diffraction, optical microscopy, and</p> <p>17 electron microscopy techniques) and its</p> <p>18 sensitivity must be provided. Even if the</p> <p>19 product is "asbestos-free," the mechanism of</p> <p>20 cancer induction by asbestos (i.e.,</p> <p>21 metal-catalyzed radical generation) is similarly</p> <p>22 pertinent to talc and the occurrence of fibrous</p> <p>23 forms of the sheet silicate itself raises issues</p> <p>24 about clearance and long-term safety. Simply</p>	<p>1 Q But you'll agree that this was out of</p> <p>2 the context of any litigation about baby powder;</p> <p>3 correct?</p> <p>4 MS. CURRY:</p> <p>5 Object to the form.</p> <p>6 A I would agree on that.</p> <p>7 MS. THOMPSON:</p> <p>8 Q What's your understanding of the</p> <p>9 mechanism by which asbestos causes cancer?</p> <p>10 MS. CURRY:</p> <p>11 Object to the form.</p> <p>12 A Again, I'm not necessarily an expert on</p> <p>13 this. The association and the risk factor's very</p> <p>14 clear. I think the present theory -- and I would</p> <p>15 put it as a theory -- is this is a substance that</p> <p>16 essentially doesn't dissolve, stays there, or at</p> <p>17 least is very long-lasting, and then, under those</p> <p>18 circumstances, causes effectively the</p> <p>19 transformation of cells that it is in close</p> <p>20 contact with. And that's -- it includes, of</p> <p>21 course, lung cancer per se, but also mesothelioma</p> <p>22 where these particles will sort of stay in the</p> <p>23 pleural cavity.</p> <p>24 MS. THOMPSON:</p>

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<p style="text-align: right;">Page 298</p> <p>1 Q Is there anything in that description 2 that you gave that would be different for talc? 3 MS. CURRY: 4 Object to the form. 5 A Well -- 6 MS. THOMPSON: 7 Q And we're speaking in general terms. 8 MS. CURRY: 9 Object to the form. 10 A Talc doesn't do this; right? 11 MS. THOMPSON: 12 Q Well, no. Let's go back. 13 You would agree that talc essentially 14 doesn't dissolve also; correct? 15 MS. CURRY: 16 Object to the form. 17 A It's a mineral. 18 MS. THOMPSON: 19 Q And it stays there; correct? 20 MS. CURRY: 21 Object to the form. 22 A Well, I don't know if it stays there as 23 long as asbestos. You know, if you look at the 24 pleurodesis patients, there's really essentially</p>	<p style="text-align: right;">Page 300</p> <p>1 because I wasn't asked to review that, and -- and 2 my experience is in lung cancer. 3 That process, I think, is still -- is 4 still questionable. And -- and because of that, 5 that -- that process may be specifically 6 associated with asbestos. So to extrapolate that 7 to some other molecule that, oh, by the way, it 8 hangs around for a while, is not acceptable. 9 Q So I understand that you apparently 10 were not asked to consider asbestos. You're a 11 scientist; right? 12 A Yes. 13 Q Did you not have any curiosity about 14 what effects the presence of asbestos in baby 15 powder would have? 16 MS. CURRY: 17 Object to the form. 18 A To be honest, that wasn't the way I 19 approached it. I approached it by looking 20 specifically from the talc standpoint. 21 MS. THOMPSON: 22 Q Okay. 23 A And -- and the studies and then looking 24 at that objectively. And, again, we get back to</p>
<p style="text-align: right;">Page 299</p> <p>1 no increase in ovarian cancer. 2 MS. THOMPSON: 3 Q Well, you've already told us that 4 pleurodesis patients have typically a life 5 expectancy of months, not years. 6 MS. CURRY: 7 Object to the form. 8 A I said in the ones I treat. But in 9 chronic heart failure, those patients have been 10 followed up to 40 years. 11 MS. THOMPSON: 12 Q I would like to see that study, but 13 we'll do that another day. How's that? 14 A I don't know if I'd like another day. 15 Q Let's say -- or -- your next comment, 16 or at least it's very long-lasting. You would 17 agree that -- with that for talc; right? 18 A Uh-huh. Uh-huh. 19 Q And, then, for asbestos, you say it 20 causes effectively the transformation of cells 21 that it's in close contact with. But you don't 22 believe that happens for talc; correct? 23 A Well, again, this may reflect my -- 24 somewhat my ignorance about asbestos per se,</p>	<p style="text-align: right;">Page 301</p> <p>1 this issue of really looking at epidemiologic 2 studies, just use powder, and then some of the 3 studies biologically used it -- use those -- used 4 those products. It -- you know, if there are -- 5 if there are substance X, Y, Z, A, B, and C that 6 are in there that are causing a problem and 7 carcinogenic, it would have shown up in the 8 studies. 9 Q Do you know that initially in the 10 studies, asbestos, no one could prove that 11 asbestos was carcinogenic? 12 MS. CURRY: 13 Object to the form. 14 A Well, no one could prove smoking was 15 carcinogenic either. It takes time. 16 MS. THOMPSON: 17 Q Well, there's two examples then. 18 (DEPOSITION EXHIBIT NUMBER 26 19 WAS MARKED FOR IDENTIFICATION.) 20 MS. THOMPSON: 21 Q I'm going to show you Exhibit 26, a 22 paper by Dr. Mossman. Do you know Mossman? 23 A I do know Dr. Mossman. Not personally. 24 Q You know her by reputation?</p>

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<p style="text-align: right;">Page 302</p> <p>1 A I think we shared classmates about 20</p> <p>2 years ago.</p> <p>3 Q I -- I won't -- I won't go any further</p> <p>4 with that one.</p> <p>5 The title of this study is "Mechanistic</p> <p>6 in vitro studies: What they have told us about</p> <p>7 carcinogenic properties of elongated mineral</p> <p>8 particles."</p> <p>9 I think we've already established that</p> <p>10 that's not a term that you're particularly</p> <p>11 familiar with. But go ahead and take a minute to</p> <p>12 look at --</p> <p>13 A 26?</p> <p>14 Q -- that paper.</p> <p>15 And I'm going to just read from the</p> <p>16 abstract. "In vitro studies using target and</p> <p>17 effector cells of mineral-induced cancers have</p> <p>18 been critical in determining the mechanisms of</p> <p>19 pathogenesis as well as the properties" --</p> <p>20 A Where are you?</p> <p>21 Q The first sentence of the paper, in the</p> <p>22 abstract.</p> <p>23 A Oh, okay. Thank you.</p> <p>24 Q "In vitro studies" -- we'll start over.</p>	<p style="text-align: right;">Page 304</p> <p>1 Object to the form.</p> <p>2 MS. THOMPSON:</p> <p>3 Q That in vitro studies could be used to</p> <p>4 test that mechanism in EMPs?</p> <p>5 A And she's --</p> <p>6 MS. CURRY:</p> <p>7 Object to the form.</p> <p>8 A -- she's well respected in this area.</p> <p>9 MS. THOMPSON:</p> <p>10 Q We're going to get to Saed's, Dr.</p> <p>11 Saed's work in a minute.</p> <p>12 A Okay.</p> <p>13 Q But wouldn't you agree that that's what</p> <p>14 Dr. Saed started testing in his in vitro studies?</p> <p>15 MS. CURRY:</p> <p>16 Object to the form.</p> <p>17 A I think the expert report and the paper</p> <p>18 that I read is within this spectrum.</p> <p>19 MS. THOMPSON:</p> <p>20 Q And, just moving down a little bit,</p> <p>21 maybe two-thirds of the way down, "Comparative</p> <p>22 studies using chemical carcinogens showed that</p> <p>23 chemical agents interacted directly with DNA;</p> <p>24 whereas, long EMPs appeared to be promoters of</p>
<p style="text-align: right;">Page 303</p> <p>1 "In vitro studies using target and</p> <p>2 effector cells of mineral-induced cancers have</p> <p>3 been critical in determining the mechanisms of</p> <p>4 pathogenesis as well as the properties of</p> <p>5 elongated mineral particles, EMPs, important in</p> <p>6 eliciting these responses."</p> <p>7 Dr. Mossman is reporting that in vitro</p> <p>8 studies have been helpful in -- in determining</p> <p>9 this mechanism; right?</p> <p>10 MS. CURRY:</p> <p>11 Object to the form.</p> <p>12 A Yeah, I think that's what she's saying.</p> <p>13 Yes.</p> <p>14 MS. THOMPSON:</p> <p>15 Q Next sentence, "Historically, in vitro</p> <p>16 models of mutagenesis and immortalized cell lines</p> <p>17 were first used to test the theory that EMPs were</p> <p>18 mutagenic to cells, and genotoxicity, as defined</p> <p>19 as damage to DNA, often culminating in cell</p> <p>20 death, was observed in a dose-dependent fashion</p> <p>21 as responses of many cell types to a number of</p> <p>22 EMPs."</p> <p>23 Does that sound reasonable?</p> <p>24 MS. CURRY:</p>	<p style="text-align: right;">Page 305</p> <p>1 cancer via a number of mechanisms, such as</p> <p>2 inflammation, generation of oxidants and</p> <p>3 instigation of cell division.</p> <p>4 "The multitude of these signaling</p> <p>5 cascades and epigenetic mechanisms of both lung</p> <p>6 cancers and mesotheliomas have been most recently</p> <p>7 studied in normal or telomerase immortalized</p> <p>8 human cells."</p> <p>9 I believe she's saying -- and I'll ask</p> <p>10 you if it's correct -- that particles,</p> <p>11 particularly the elongated particles or fibers,</p> <p>12 have a different mechanism than what is usually</p> <p>13 thought of with chemical carcinogens.</p> <p>14 MS. CURRY:</p> <p>15 Object to the form.</p> <p>16 MS. THOMPSON:</p> <p>17 Q Is that a --</p> <p>18 A I think that's --</p> <p>19 Q -- reasonable interpretation?</p> <p>20 A You know, again, we've been down this</p> <p>21 road a little bit. This is a review article, so</p> <p>22 she's kind of looking at it globally. But I</p> <p>23 think that what you describe is one of the, sort</p> <p>24 of, take-home messages she's implying.</p>

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<p style="text-align: right;">Page 306</p> <p>1 Q Thank you. I'm honored --</p> <p>2 A Okay. We're done?</p> <p>3 Q -- to have kind of gotten it right.</p> <p>4 A We're done?</p> <p>5 Q No.</p> <p>6 A No?</p> <p>7 Q But I'm gonna shave 10 minutes off for</p> <p>8 that compliment.</p> <p>9 And in the paragraph 2, "General</p> <p>10 Concepts of Cancer Development," first</p> <p>11 paragraph --</p> <p>12 MS. CURRY:</p> <p>13 I'm sorry. The realtime is not --</p> <p>14 (Off the record.)</p> <p>15 A I wouldn't -- we -- can we sort of edge</p> <p>16 towards a break at some point?</p> <p>17 MS. THOMPSON:</p> <p>18 Q Yeah. Let's just go ahead and just</p> <p>19 finish -- almost finished, and then we'll come</p> <p>20 back. That's a good -- good spot.</p> <p>21 (Technical difficulties with realtime.)</p> <p>22 MS. THOMPSON:</p> <p>23 Q Are we okay going forward for a couple</p> <p>24 questions without the realtime?</p>	<p style="text-align: right;">Page 308</p> <p>1 MS. THOMPSON:</p> <p>2 Q Would you agree that some scientists</p> <p>3 tend to like one explanation or the other, and</p> <p>4 the other scientists liking a different</p> <p>5 explanation more than the first one?</p> <p>6 MS. CURRY:</p> <p>7 Object to the form.</p> <p>8 A I think that -- I think if you look at</p> <p>9 the investigators in this field, they'll come at</p> <p>10 it, as their expertise, from one direction or the</p> <p>11 other.</p> <p>12 But, you know -- you know, Brook is</p> <p>13 somebody who sees the big picture. I'd like to</p> <p>14 think I do, too. So there's some of us who look</p> <p>15 at the whole thing.</p> <p>16 MS. THOMPSON:</p> <p>17 Q Okay. That's a good explanation.</p> <p>18 But there are scientists doing credible</p> <p>19 work that are kind of in both camps?</p> <p>20 MS. CURRY:</p> <p>21 Object to the form.</p> <p>22 A I think that's fair.</p> <p>23 MS. THOMPSON:</p> <p>24 Q And then I'm going to that next page.</p>
<p style="text-align: right;">Page 307</p> <p>1 A Yes.</p> <p>2 Q So in number 2, "General Concepts of</p> <p>3 Cancer Development."</p> <p>4 A Uh-huh.</p> <p>5 Q "The development and use of in vitro</p> <p>6 models over time has corresponded with the</p> <p>7 evolution of research and knowledge on cancer</p> <p>8 etiology in humans."</p> <p>9 Would you agree with that statement?</p> <p>10 A I think so, yes.</p> <p>11 Q Next sentence, "While some scientists</p> <p>12 have suggested that the relative contributions of</p> <p>13 DNA replications and mutations are overwhelming</p> <p>14 drivers of cancer risk, others argue that</p> <p>15 experimental and evolutionary data point to</p> <p>16 tissue microenvironment and epigenetic changes as</p> <p>17 being key to tumorigenesis."</p> <p>18 Would you agree with that statement?</p> <p>19 MS. CURRY:</p> <p>20 Object to the form.</p> <p>21 A I think it's a quantitative issue. So</p> <p>22 in some tumors, mutagenesis takes prominence; in</p> <p>23 others, the microenvironment is important. And</p> <p>24 it's a spectrum.</p>	<p style="text-align: right;">Page 309</p> <p>1 I just have, I think, one more passage I'd like</p> <p>2 to read from this paper and get -- get your</p> <p>3 thoughts.</p> <p>4 The first full paragraph on the second</p> <p>5 page of the article, page 63, "The modern day</p> <p>6 definition of epigenetic mechanisms has evolved</p> <p>7 over time to encompass the fact that alterations</p> <p>8 in the primary structure of DNA do not underlie</p> <p>9 most changes in the development of tumors.</p> <p>10 Accordingly, an epigenetic trait can be a stable</p> <p>11 inheritable phenotype resulting from changes in a</p> <p>12 chromosome without alteration in the DNA</p> <p>13 sequence."</p> <p>14 Do you agree with that statement?</p> <p>15 MS. CURRY:</p> <p>16 Object to the form.</p> <p>17 A It strikes me as a little overstated,</p> <p>18 particularly the first part, "...epigenetic</p> <p>19 mechanism evolved over time to encompass the fact</p> <p>20 that alterations in the primary structure do not</p> <p>21 underline most changes." That, I -- I'm not sure</p> <p>22 where that's coming from.</p> <p>23 Now, it may be in a single tumor,</p> <p>24 epigenetic is more important than mutation; but</p>

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<p style="text-align: right;">Page 310</p> <p>1 in others, a mutation would be more important. 2 Again, when we treat patients, as you 3 know, we're sequencing everything, and that's not 4 looking at epigenetics. It's looking at 5 mutations. Tumors are riddled with these things. 6 In fact, the problem that we face is what's the 7 driver versus the passenger. 8 MS. THOMPSON: 9 Q So in a particular tumor, either 10 mechanism -- well, it could be either mechanism 11 or both in various amount of contribution. Is 12 that a fair statement? 13 MS. CURRY: 14 Object to the form. 15 A I think it's a fair statement. 16 MS. THOMPSON: 17 Let's take a break. 18 VIDEOGRAPHER: 19 Off the record at 3:26 p.m. 20 (OFF THE RECORD.) 21 VIDEOGRAPHER: 22 We're back on the record at 3:45 p.m. 23 MS. THOMPSON: 24 Q Dr. Birrer, let's talk about Dr. Saed</p>	<p style="text-align: right;">Page 312</p> <p>1 So -- and then he did a fair amount of work on 2 adhesion, pure adhesion. 3 MS. THOMPSON: 4 Q And his adhesion work involved 5 oxidative stress in adhesions, didn't it? 6 A I think he would argue that. I 7 didn't -- it wasn't clear to me from my 8 perspective. But that's a component of what he 9 looked at. The unifying factor for me is that 10 it's gynecologic. 11 Q Okay. 12 A Okay. 13 Q And he has 234 peer-reviewed 14 publications; correct? Oh, no. Take that back. 15 A 136, isn't it? 16 Q 136. I was looking -- 17 A 136. Correct. 18 Q What is oxidative stress? 19 A Well, that's -- that's a biochemical 20 state, if you will, within -- we -- we consider 21 as biologists within cells. It exists in all 22 cells. And it's a balance between ox- -- you 23 know, oxidizing effects and antioxidants. 24 As a term, oxidative, of course, it's a</p>
<p style="text-align: right;">Page 311</p> <p>1 and his research. Okay? 2 A Okay. 3 Q Did you look at Dr. Saed's CV? 4 A I did. 5 Q I'll go ahead and mark that as exhibit 6 27. 7 (DEPOSITION EXHIBIT NUMBER 27 WAS 8 MARKED FOR IDENTIFICATION.) 9 A Thank you. 10 MS. THOMPSON: 11 Q And looking at his CV, would you agree 12 that the focus of his lab has been the study of 13 oxidative stress and its biological effects? 14 MS. CURRY: 15 Object to the form. 16 A Let me refresh my -- refresh my memory 17 on this a little bit. 18 So I think, you know, looking at, if I 19 recall correctly -- I would say that he -- one of 20 his -- one of the components of what he looks at 21 is oxidative stress. If you look at his career, 22 he's been fairly broadly over a broad number of 23 topics. He's looked at, like, gene amplification 24 in certain tumors, mostly in GYN, I might add.</p>	<p style="text-align: right;">Page 313</p> <p>1 chemistry definition. But this one, I think what 2 he means by oxidative stress is it's -- or what 3 you're implying is it's a biologic process. 4 Okay? 5 Q And is it fair to say that at least 6 some scientists believe that oxidative stress 7 plays a role in the etiology of many types of 8 cancers? 9 MS. CURRY: 10 Object to the form. 11 A I think it's safe to say oxidative 12 stress has been investigated and associated with 13 some cancers. 14 MS. THOMPSON: 15 Q Okay. Do you have an opinion on the 16 role of oxidative stress in the initiation of 17 ovarian cancer? 18 A I think that's unresolved at this 19 point. Most of the data that I know of for 20 oxidative stress, a lot of the data is in ovarian 21 tumors. They're already established. 22 Q Are -- would you say there are 23 scientists on both sides of that issue? 24 MS. CURRY:</p>

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<p>1 Object to the form.</p> <p>2 A Would you define that, please?</p> <p>3 MS. THOMPSON:</p> <p>4 Q The importance of oxidative stress in</p> <p>5 the pathogenesis of ovarian cancer.</p> <p>6 MS. CURRY:</p> <p>7 Object to the form.</p> <p>8 A I think it's an area of active</p> <p>9 investigation.</p> <p>10 MS. THOMPSON:</p> <p>11 Q Okay. So you would agree that</p> <p>12 researchers who believe that oxidative stress</p> <p>13 plays a role in the initiation or progression of</p> <p>14 ovarian cancer are not unreasonable?</p> <p>15 MS. CURRY:</p> <p>16 Object to the form.</p> <p>17 A It's a generalization that I can't</p> <p>18 comment on. Which researchers?</p> <p>19 MS. THOMPSON:</p> <p>20 Q Okay. But they wouldn't automatically</p> <p>21 be unreasonable?</p> <p>22 MS. CURRY:</p> <p>23 Object to the form.</p> <p>24 A Because they believe --</p>	<p>1 A Yeah.</p> <p>2 Q Let's go to your report.</p> <p>3 A We're done with the CV?</p> <p>4 Q I think so.</p> <p>5 A Are you going to the report or the</p> <p>6 paper?</p> <p>7 Q I'm going to your report first.</p> <p>8 A Yeah. Okay.</p> <p>9 Q And then the report, I'll probably go</p> <p>10 to the -- this paper next.</p> <p>11 So in your report, going to page --</p> <p>12 actually, let's start on page 19.</p> <p>13 A Uh-huh.</p> <p>14 Q And you have the big heading, Section</p> <p>15 4 --</p> <p>16 A Uh-huh.</p> <p>17 Q -- Dr. Saed's Plaintiff-Funded</p> <p>18 Research.</p> <p>19 Did you write that heading?</p> <p>20 A Yes.</p> <p>21 Q What is the basis for calling</p> <p>22 Dr. Saed's research plaintiff-funded?</p> <p>23 A My understanding is after he submitted</p> <p>24 his -- the preprint said -- revealed,</p>
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<p>1 MS. THOMPSON:</p> <p>2 Q Because they believe in the importance</p> <p>3 of oxidative stress.</p> <p>4 A I don't think so.</p> <p>5 Q They wouldn't automatically be</p> <p>6 credible -- not credible?</p> <p>7 MS. CURRY:</p> <p>8 Object to the form.</p> <p>9 A That would depend on the work they've</p> <p>10 done --</p> <p>11 MS. THOMPSON:</p> <p>12 Q Okay.</p> <p>13 A -- in their experiments.</p> <p>14 Q All right. And they wouldn't</p> <p>15 automatically be uninformed. Would you agree</p> <p>16 with that?</p> <p>17 MS. CURRY:</p> <p>18 Object to the form.</p> <p>19 MS. THOMPSON:</p> <p>20 Q It would depend?</p> <p>21 A We need to look at their -- their</p> <p>22 scientific investigation to determine if they're</p> <p>23 uninformed.</p> <p>24 Q Okay.</p>	<p>1 essentially, nothing, and then the actual paper,</p> <p>2 I believe, said that he was -- that he was a</p> <p>3 consultant and an expert witness.</p> <p>4 Q Does that mean to you plaintiff-funded</p> <p>5 research?</p> <p>6 A Well, I mean, that was a separate</p> <p>7 issue, that there was money actually flowing into</p> <p>8 his lab.</p> <p>9 Q What -- what is your basis for saying</p> <p>10 there was money flowing into his lab?</p> <p>11 A I think that's what we -- I saw in</p> <p>12 his -- let me see. Hang on -- his deposition.</p> <p>13 Q What did his deposition say about that?</p> <p>14 A I'd have to refresh my memory. Do you</p> <p>15 have it?</p> <p>16 Q Do you recall that the funding for the</p> <p>17 research came from his university lab funds and</p> <p>18 that he was paid for his time as a consultant?</p> <p>19 Does that sound right?</p> <p>20 MS. CURRY:</p> <p>21 Object to the form.</p> <p>22 A I think I remember that the exchange</p> <p>23 was he was saying his departmental monies and</p> <p>24 then he was asked, okay, where does that come</p>

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<p>1 from, and he couldn't answer that and said, well,</p> <p>2 I don't know. And the problem is --</p> <p>3 MS. THOMPSON:</p> <p>4 Q That's -- that's just not right.</p> <p>5 A Okay. Can we look at it?</p> <p>6 Q And I don't have his deposition here.</p> <p>7 But to put as your heading "Dr. Saed's</p> <p>8 Plaintiff-Funded Research" without really knowing</p> <p>9 the situation is -- doesn't sound like something</p> <p>10 you would write in a paper.</p> <p>11 MS. CURRY:</p> <p>12 Object to the form.</p> <p>13 A No.</p> <p>14 MS. THOMPSON:</p> <p>15 Q Does it?</p> <p>16 A In a peer-review paper?</p> <p>17 Q Right.</p> <p>18 A No. But this is not a peer-review</p> <p>19 paper.</p> <p>20 Q Well, did you not --</p> <p>21 A The fact that he has plaintiff-funded</p> <p>22 research and hasn't really revealed it is a huge</p> <p>23 issue.</p> <p>24 Q What -- what's your basis for saying he</p>	<p>1 A Yeah.</p> <p>2 Q -- the published manuscript.</p> <p>3 (DEPOSITION EXHIBIT NUMBER 28</p> <p>4 WAS MARKED FOR IDENTIFICATION.)</p> <p>5 MS. THOMPSON:</p> <p>6 Q Have you seen that?</p> <p>7 A I have seen this, yes.</p> <p>8 Q And you're talking about the conflict</p> <p>9 of interest statement; correct?</p> <p>10 A Yes.</p> <p>11 Q Doctor -- I'm sorry. Exhibit 28 is his</p> <p>12 manuscript.</p> <p>13 And the declaration of conflicting</p> <p>14 interests.</p> <p>15 A Uh-huh.</p> <p>16 Q "Dr. Saed has served as a paid</p> <p>17 consultant and expert witness in the talcum</p> <p>18 litigation."</p> <p>19 Is -- is that a reason to make the</p> <p>20 heading of your report "Dr. Saed's</p> <p>21 Plaintiff-Funded Research"?</p> <p>22 MS. CURRY:</p> <p>23 Object to the form.</p> <p>24 A Well, I think -- so I guess the</p>
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<p>1 hasn't revealed it?</p> <p>2 A It's not on the manuscript.</p> <p>3 Q The manuscript that's published?</p> <p>4 A Yeah.</p> <p>5 Q Well, let's look at the manuscript.</p> <p>6 So is your criticism that it's not on</p> <p>7 the manuscript or that it's plaintiff-funded</p> <p>8 research?</p> <p>9 MS. CURRY:</p> <p>10 Object to the form.</p> <p>11 A Well, it's two. Yeah.</p> <p>12 MS. THOMPSON:</p> <p>13 Q Because there's nothing in that heading</p> <p>14 that says this research -- I just -- I just don't</p> <p>15 understand the heading "Dr. Saed's</p> <p>16 Plaintiff-Funded Research."</p> <p>17 A So I think there's two components</p> <p>18 there. One is I think it is an issue that --</p> <p>19 that there's dollars flowing to do some of that</p> <p>20 research. I think that raises an issue of how</p> <p>21 objective he is.</p> <p>22 And then a second issue is at a minimum</p> <p>23 it should be revealed.</p> <p>24 Q Now, this is --</p>	<p>1 question is: Is this accurate? This was not on</p> <p>2 the preprint. This was not on the --</p> <p>3 MS. THOMPSON:</p> <p>4 Q This is what's published; right?</p> <p>5 A That's not a preprint.</p> <p>6 Q Do you know what correspondence</p> <p>7 Dr. Saed -- or what -- what are you speaking of?</p> <p>8 The submission to --</p> <p>9 A The paper was submitted to GYN ONC and</p> <p>10 rejected, and then the paper was submitted to --</p> <p>11 this is Reproductive Sciences. And those --</p> <p>12 again, do we have a copy of that? I got the</p> <p>13 preprint which stated -- which said none of that.</p> <p>14 Q Okay. We'll get to that in a minute.</p> <p>15 A This was only put on afterwards.</p> <p>16 Q Do you have any -- do you have any</p> <p>17 knowledge of the conversations that Dr. Saed had</p> <p>18 with the editors of either journal as to what</p> <p>19 should go on his conflict of interest statement</p> <p>20 with the situation that he was in?</p> <p>21 Do you have any knowledge of that</p> <p>22 whatsoever?</p> <p>23 A Verbal conversations.</p> <p>24 Q Written and verbal conversations.</p>

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<p>1 A So verbal conversations, I don't know. 2 I'm not there. The written interactions between 3 the journals, we had copies of. 4 Q And you think what you saw was 5 sufficient enough for you to state "Dr. Saed's 6 Plaintiff-Funded Research" in this report? 7 A I think so, yeah. It's a big issue. 8 Q Wouldn't a scientist want to look at 9 the research before they call it plaintiff-funded 10 research? 11 MS. CURRY: 12 Object to the form. 13 MS. THOMPSON: 14 Q Doesn't that automatically indicate 15 that you think the research is biased? 16 A Well, again, I -- so as this document 17 evolved, I looked at the science and I -- I was 18 chagrined. That then put this into context. I 19 think -- I think it's a concern. 20 Q Well, couldn't you have just said 21 "Dr. Saed's Research" and then written your 22 comments without making the heading 23 "Plaintiff-Funded Research"? 24 MS. CURRY:</p>	<p>1 actual research in the lab, is that -- 2 A I can't quite -- 3 MS. CURRY: 4 Object to the form. 5 A I can't quite remember. 6 MS. THOMPSON: 7 Q Okay. 8 A But -- 9 Q So -- 10 A It was a big position. 11 Q So do you think that heading is fair? 12 A I think it is. 13 Q Do you remember Dr. Saed's testimony 14 that he would have been -- that he would have 15 been happy to do the same research had 16 Johnson & Johnson approached him on the same 17 topic? 18 MS. CURRY: 19 Object to the form. 20 A I can't remember. Do you have the 21 deposition? 22 MS. THOMPSON: 23 Q I don't. 24 A Okay.</p>
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<p>1 Object to the form. 2 A I could have. 3 MS. THOMPSON: 4 Q Isn't there plenty of research being 5 done that's funded by various entities that's 6 quality research? 7 A So there's a broad spectrum of -- 8 Q Answer my question. Isn't there a lot 9 of research that's being done funded by various 10 entities that's quality research? 11 A As a general statement? 12 Q Uh-huh. 13 A Yes. 14 Q Yes. 15 And funding has to come from somewhere; 16 correct? 17 MS. CURRY: 18 Object to the form. 19 A Can't work without money. 20 MS. THOMPSON: 21 Q And, again, you may not remember this 22 from Dr. Saed's deposition, but his testimony 23 that there was no money coming from the 24 litigation into his lab funds which paid for the</p>	<p>1 Q You don't remember that he said his 2 research would have been the same and he would 3 have been willing to do it for Johnson & Johnson? 4 MS. CURRY: 5 Object to the form. 6 A I can't remember it. 7 MS. THOMPSON: 8 Q To your knowledge, has 9 Johnson & Johnson approached any researcher about 10 doing studies that would help understand whether 11 talcum powder has any molecular effects? 12 MS. CURRY: 13 Object to the form. 14 A He certainly didn't approach me. But 15 I -- I think I recall in the past they've had a 16 J & J-funded study, I think, which was 17 acknowledged on the paper. 18 MS. THOMPSON: 19 Q A molecular study? 20 A I can't say that. 21 Q If you had that, I would certainly like 22 to see it. So, to your knowledge, 23 Johnson & Johnson hasn't asked -- has not asked 24 any researchers to look at the molecular effects</p>

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<p>1 of talcum powder in cell culture?</p> <p>2 A Outside the company, right?</p> <p>3 Q How about inside the company?</p> <p>4 A I don't know. I don't know what goes</p> <p>5 on there.</p> <p>6 Q Did you ask the attorneys --</p> <p>7 A No.</p> <p>8 Q -- if Johnson & Johnson had done any</p> <p>9 studies that you could look at and --</p> <p>10 A No.</p> <p>11 Q -- criticize in the same way you did</p> <p>12 Dr. Saed?</p> <p>13 MS. CURRY:</p> <p>14 Object to the form.</p> <p>15 A Well, I wouldn't rely on those, the</p> <p>16 internal documents. I would have to know the</p> <p>17 context.</p> <p>18 MS. THOMPSON:</p> <p>19 Q Well, can't you --</p> <p>20 A But this is -- this is peer-reviewed.</p> <p>21 Q Can't you find the context of -- of</p> <p>22 what studies have been done by the company?</p> <p>23 A I think that would be hard.</p> <p>24 Q So it would be of no interest to you</p>	<p>1 A No.</p> <p>2 Q Did you have any conversations by</p> <p>3 email, text or phone with the editors or any</p> <p>4 other representatives of the journal regarding</p> <p>5 this paper?</p> <p>6 A No.</p> <p>7 Q Did you have any conversations with</p> <p>8 Johnson & Johnson regarding the manuscript while</p> <p>9 it was under review?</p> <p>10 A No.</p> <p>11 Q Did you have any conversations with any</p> <p>12 of the reviewers on the paper?</p> <p>13 A I don't know who the reviewers were.</p> <p>14 Q Okay.</p> <p>15 A Yeah.</p> <p>16 Q But you have seen the reviewer comments</p> <p>17 from GYN Oncology; correct?</p> <p>18 A I did.</p> <p>19 Do we have a copy?</p> <p>20 MS. CURRY:</p> <p>21 I think she's --</p> <p>22 MS. THOMPSON:</p> <p>23 Yeah, I'm --</p> <p>24 (DEPOSITION EXHIBIT NUMBER 29 WAS</p>
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<p>1 one way or the other whether Johnson & Johnson</p> <p>2 had done any molecular studies on talcum powder</p> <p>3 and its effect on -- on tissue or cells?</p> <p>4 A Correct.</p> <p>5 MS. CURRY:</p> <p>6 Object to the form.</p> <p>7 A Correct.</p> <p>8 MS. THOMPSON:</p> <p>9 Q When did you -- is the paper that we</p> <p>10 just marked as exhibit --</p> <p>11 A 28.</p> <p>12 Q -- 28, was that paper peer-reviewed?</p> <p>13 A This is a peer-review journal.</p> <p>14 Q And when did you first see the</p> <p>15 unpublished manuscript?</p> <p>16 A I am gonna really -- I'm stretching on</p> <p>17 this. I think it was about -- let's say a month</p> <p>18 or two before this.</p> <p>19 Q Okay. So a couple months ago?</p> <p>20 A Yeah.</p> <p>21 Q Do you review papers for Gynecologic</p> <p>22 Oncology?</p> <p>23 A I do.</p> <p>24 Q Were you asked to review this paper?</p>	<p>1 MARKED FOR IDENTIFICATION.)</p> <p>2 MS. THOMPSON:</p> <p>3 Q I'm gonna go ahead and mark Exhibit 29.</p> <p>4 29 will be the reviewer comments from the journal</p> <p>5 Gynecologic Oncology.</p> <p>6 A Uh-huh.</p> <p>7 Q And again, that journal is the</p> <p>8 journal -- or maybe we haven't discussed this --</p> <p>9 it's the journal for SGO, the Society of</p> <p>10 Gynecologic Oncologists; correct?</p> <p>11 A Correct.</p> <p>12 Q Did I give you a highlighted copy?</p> <p>13 A You did, actually. It's very helpful.</p> <p>14 Q Let me switch that. I'm sure it was.</p> <p>15 Actually, it probably wasn't.</p> <p>16 A I've seen these before.</p> <p>17 (DEPOSITION EXHIBIT NUMBER 30 WAS</p> <p>18 MARKED FOR IDENTIFICATION.)</p> <p>19 MS. THOMPSON:</p> <p>20 Q And then I'm gonna also, at the same</p> <p>21 time, give you Exhibit 30, which is the reviewer</p> <p>22 comments from Reproductive Sciences.</p> <p>23 A All right.</p> <p>24 Q Both are peer-reviewed journals, as you</p>

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<p>1 mentioned; right?</p> <p>2 A Yes. Difference in impact, but both</p> <p>3 peer review.</p> <p>4 Q And they have a -- a different audience</p> <p>5 readership, too, wouldn't you agree?</p> <p>6 A I would agree, yes.</p> <p>7 MS. CURRY:</p> <p>8 Do you have another copy of Exhibit 30?</p> <p>9 MS. THOMPSON:</p> <p>10 Yes. I'm sorry.</p> <p>11 MS. CURRY:</p> <p>12 Thank you.</p> <p>13 MS. THOMPSON:</p> <p>14 That good?</p> <p>15 MS. CURRY:</p> <p>16 Yes.</p> <p>17 MS. THOMPSON:</p> <p>18 Q In your report, you make the statement</p> <p>19 "Unsurprisingly, this manuscript has serious</p> <p>20 methodologic, experimental and analysis flaws."</p> <p>21 A I'm sorry. Are you in the beginning of</p> <p>22 this last paragraph of 19?</p> <p>23 Q No.</p> <p>24 A No?</p>	<p>1 Q Reading the letter to Dr. Saed:</p> <p>2 "Your paper, referenced above, has now</p> <p>3 been reviewed by at least two reviewers -- has</p> <p>4 now been reviewed by at least two experts in the</p> <p>5 field and the editors. Based on the reviewer</p> <p>6 comments, we must inform you that while your work</p> <p>7 is not without merit, we are unable to accept</p> <p>8 your manuscript for publication in Gynecologic</p> <p>9 Oncology. In the last year we have seen a</p> <p>10 significant increase in the number of manuscripts</p> <p>11 submitted to the journal, and, as a result, we</p> <p>12 are now accepting less than 20 percent of the</p> <p>13 manuscripts submitted to the Gynecologic</p> <p>14 Oncology."</p> <p>15 Certainly in that first paragraph there</p> <p>16 were -- there was no language that resembles this</p> <p>17 manuscript has serious methodologic, experimental</p> <p>18 and analysis flaws, is there?</p> <p>19 A No.</p> <p>20 Q The second paragraph, "We have attached</p> <p>21 the comments of the reviewers below in order for</p> <p>22 you to understand the basis for our decision. We</p> <p>23 hope that their thoughtful comments will help you</p> <p>24 in your future studies and possibly with</p>
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<p>1 Q It's in another spot. Let me find it.</p> <p>2 A Maybe it's under the paper.</p> <p>3 Q Yeah. Page 24.</p> <p>4 A Yep. Yeah.</p> <p>5 Q "Unsurprisingly, this manuscript has</p> <p>6 serious methodologic, experimental and analysis</p> <p>7 flaws."</p> <p>8 A Uh-huh.</p> <p>9 Q Did you see any language to that effect</p> <p>10 in the peer-reviewers' comments?</p> <p>11 MS. CURRY:</p> <p>12 Object to the form.</p> <p>13 A One second.</p> <p>14 MS. THOMPSON:</p> <p>15 Q Well, let me just ask you.</p> <p>16 Did those words appear in the reviewer</p> <p>17 comments?</p> <p>18 A No, I don't think so.</p> <p>19 Q Okay.</p> <p>20 A Yeah.</p> <p>21 Q So let's -- I want to actually go</p> <p>22 through the reviewer comments. We'll start with</p> <p>23 Gynecologic Oncology.</p> <p>24 A Yep.</p>	<p>1 submission to another journal.</p> <p>2 "Please note that a revised version of</p> <p>3 the current manuscript should not be submitted</p> <p>4 for another review to Gynecologic Oncology."</p> <p>5 There's certainly no language in that</p> <p>6 paragraph that resembles serious methodologic,</p> <p>7 experimental and analysis flaws, is there?</p> <p>8 A No.</p> <p>9 Q And the reviewers actually encouraged</p> <p>10 Dr. Saed to submit the article to another</p> <p>11 journal; correct?</p> <p>12 A Well, this isn't the reviewer. This is</p> <p>13 the editor.</p> <p>14 Q The editor?</p> <p>15 A Yeah.</p> <p>16 Q The editors?</p> <p>17 A Yeah. And this is boilerplate. You'd</p> <p>18 always get this. They're not --</p> <p>19 Q Well, I'm just asking you for the --</p> <p>20 for what the -- what the letter says.</p> <p>21 A Yeah. Yeah.</p> <p>22 Q "The critique of this letter in no way</p> <p>23 implies a lack of interest in this area of</p> <p>24 research and we invite you to submit your future</p>

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<p style="text-align: right;">Page 334</p> <p>1 work to the journal." 2 Is that what the letter from 3 Dr. Bristow, the editor says? 4 A Correct. 5 Q And, in fact, Dr. Saed has published 6 several times in this journal previously. 7 Are you aware of that? 8 A Yeah. I believe so, yeah. 9 Q So let's go ahead and go through the -- 10 the reviewer comments. Reviewer number 1 -- 11 And, as you testified, you don't know 12 who these reviewers are; correct? 13 A I don't. 14 Q Reviewer 1, in his summary of 15 Dr. Saed's paper, says "The stated objective of 16 the study by Fletcher and colleagues is to 17 determine the effects of talc on expression of 18 key inflammatory and redox markers in ovarian 19 cancer and normal cell lines. Normal ovarian and 20 EOC cells were treated with various doses of talc 21 for 48 hours. Levels of CA-125 and selected key 22 redox enzymes were measured using realtime P -- 23 RT-PCR and ELISA." 24 Is that an accurate statement of what</p>	<p style="text-align: right;">Page 336</p> <p>1 MS. THOMPSON: 2 Q Right. 3 A Yeah. 4 Q "This is an important but controversial 5 topic in need of rigorous scientific inquiry." 6 Why is this a controversial topic, in 7 your mind? 8 MS. CURRY: 9 Object to the form. 10 MS. THOMPSON: 11 Q Or is it a controversial topic to you? 12 A I would assume they're referring to the 13 potential role of talc in ovarian cancer. But 14 I'm -- again, it's speculative. 15 Q Okay. 16 A I'm guessing. 17 Q So you wouldn't know why it would be 18 considered controversial? 19 MS. CURRY: 20 Object to the form. 21 A No. Not -- not in -- no, vis-à-vis 22 from what the reviewer's saying. 23 MS. THOMPSON: 24 Q "The current in vitro study does" --</p>
<p style="text-align: right;">Page 335</p> <p>1 the objective of the study was? 2 MS. CURRY: 3 Object to the form. 4 A I think that's -- I think that's a 5 little terse, but it covers the bases. 6 MS. THOMPSON: 7 Q And then beginning with the reviewer 8 comments, reviewer number 1 says "Overall, this 9 is a well-written manuscript and the conclusions 10 are supported by the results." 11 Do you disagree with that comment by 12 reviewer number 1? 13 A That's very generous. I don't agree 14 with it. Particularly the latter part. 15 Q But at least that's what the 16 reviewer -- 17 A Correct. 18 Q -- who was -- you would think was 19 chosen because of their expertise in the field, 20 those are the reviewer comments regarding 21 Dr. Saed's paper; correct? 22 MS. CURRY: 23 Object to the form. 24 A For reviewer 1.</p>	<p style="text-align: right;">Page 337</p> <p>1 reading on, "The current in vitro study does 2 provide novel information, but there are also 3 some important limitations described below." 4 Would you agree that it's common to 5 have a back-and-forth with a reviewer and author 6 before publication of a paper? 7 MS. CURRY: 8 Object to the form. 9 A Some papers are accepted de novo, but 10 it's unusual. Usually there are criticisms and, 11 then you'd have to revise. Sometimes if it's 12 Cancer Cell, it goes back and forth for two 13 years. 14 MS. THOMPSON: 15 Q The reviewer number 1 in -- in the 16 bullet point number 1, said "The significance of 17 the study would be greatly enhanced if a mouse 18 model corroborated the cell line findings." 19 I would -- I'm guessing you're gonna 20 agree with that statement? 21 A I do. 22 Q But you would also agree, I think, that 23 oftentimes you -- a researcher would start with 24 an in vitro study; correct?</p>

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<p>1 A Frequently.</p> <p>2 MS. CURRY:</p> <p>3 Object to the form.</p> <p>4 MS. THOMPSON:</p> <p>5 Q And what would the reasons for that be?</p> <p>6 A It's usually easier.</p> <p>7 Q Less costly?</p> <p>8 MS. CURRY:</p> <p>9 Object to the form.</p> <p>10 A By definition.</p> <p>11 MS. THOMPSON:</p> <p>12 Q And could be completed in less time?</p> <p>13 MS. CURRY:</p> <p>14 Object to the form.</p> <p>15 A Usually, yeah.</p> <p>16 MS. THOMPSON:</p> <p>17 Q Do you -- do you have any idea or</p> <p>18 knowledge of what experiments Dr. Saed is</p> <p>19 currently doing in the -- in the area of talcum</p> <p>20 powder and its biologic effects?</p> <p>21 MS. CURRY:</p> <p>22 Object to the form.</p> <p>23 A I don't.</p> <p>24 MS. THOMPSON:</p>	<p>1 A I'm not done with my response.</p> <p>2 So let me finish the first statement.</p> <p>3 Q Okay.</p> <p>4 A I think if you could show a phenom- --</p> <p>5 if you could show the biologic effects in a mouse</p> <p>6 model, then it's much stronger data, regardless</p> <p>7 of the cell lines.</p> <p>8 I don't -- I would agree I don't think</p> <p>9 Dr. Saed said much about CA-125 being -- being</p> <p>10 involved in ovarian cancer development, and</p> <p>11 that's the point. I don't understand, and I</p> <p>12 think a lot of other of us who have looked at</p> <p>13 this, don't understand what the value is of the</p> <p>14 increase in CA-125.</p> <p>15 Q Do you know that when Dr. Saed</p> <p>16 presented the initial data at the meeting, that</p> <p>17 the attendees requested that he perform CA-125</p> <p>18 and that's why he performed it? Do you remember</p> <p>19 seeing that in his deposition?</p> <p>20 MS. CURRY:</p> <p>21 Object to the form.</p> <p>22 A I didn't see that. Which meeting was</p> <p>23 this? Do you know?</p> <p>24 MS. THOMPSON:</p>
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<p>1 Q In this reviewer's opinion, "The cell</p> <p>2 line studies alone and the increase in CA-125,</p> <p>3 while intriguing, are not sufficiently</p> <p>4 convincing."</p> <p>5 Would you agree with that statement?</p> <p>6 A Absolutely.</p> <p>7 Q And so a mouse model corroboration of</p> <p>8 the findings would be -- would enhance the</p> <p>9 results; correct?</p> <p>10 A Not from my perspective. And I'm not</p> <p>11 so sure this reviewer's implying that. I think</p> <p>12 there's a real question anything can be</p> <p>13 interpreted from the cell line studies, and any</p> <p>14 increase in CA-125 is meaningless because CA-125</p> <p>15 is a marker.</p> <p>16 So I think --</p> <p>17 Q Well, wait a minute.</p> <p>18 Did Dr. Saed say anything about</p> <p>19 CA-125 --</p> <p>20 MS. CURRY:</p> <p>21 Are you done with your response?</p> <p>22 MS. THOMPSON:</p> <p>23 Q -- being the significance with the</p> <p>24 findings?</p>	<p>1 Q SRI, 2018.</p> <p>2 A Okay.</p> <p>3 Q Society of Reproductive Investigators.</p> <p>4 A And did they indicate -- anybody</p> <p>5 indicate what the purpose of that was?</p> <p>6 Q I can't tell you that.</p> <p>7 But, listen, I'm -- I'm just reading</p> <p>8 the reviewer's comments --</p> <p>9 A Yeah.</p> <p>10 Q -- without either one of us trying to</p> <p>11 speculate on what he means.</p> <p>12 But the statement is "The significance</p> <p>13 of this study would be greatly enhanced if a</p> <p>14 mouse model corroborated the cell line findings."</p> <p>15 So there were cell line findings to be</p> <p>16 corroborated; correct?</p> <p>17 A Correct.</p> <p>18 Q The reviewer number 1 also said "The</p> <p>19 significance of SNP alterations" -- that's SNP,</p> <p>20 all capitalized -- "should be further clarified."</p> <p>21 And I think you would agree with that;</p> <p>22 correct?</p> <p>23 MS. CURRY:</p> <p>24 Object to the form.</p>

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<p style="text-align: right;">Page 342</p> <p>1 A I strongly agree with that.</p> <p>2 MS. THOMPSON:</p> <p>3 Q And the viewer -- reviewer commented,</p> <p>4 "The first bulleted highlight, Oxidative Stress,</p> <p>5 is a key mechanism to the initiation and</p> <p>6 progression of ovarian cancer is not supported by</p> <p>7 this investigation and should be omitted."</p> <p>8 Does the reviewer comment on why that</p> <p>9 should be -- that line should be omitted, other</p> <p>10 than it wasn't supported by this investigation</p> <p>11 with talcum powder?</p> <p>12 A No. It would be speculative. It's --</p> <p>13 it's as you read it.</p> <p>14 Q Okay. Do you know that -- that</p> <p>15 virtually that exact statement has been published</p> <p>16 in this same journal in the past by Dr. Saed and</p> <p>17 others?</p> <p>18 MS. CURRY:</p> <p>19 Object to the form.</p> <p>20 A As a stand-alone statement?</p> <p>21 MS. THOMPSON:</p> <p>22 Q Yeah. Yes.</p> <p>23 A Yeah. I don't think that addresses</p> <p>24 what the reviewer is saying.</p>	<p style="text-align: right;">Page 344</p> <p>1 Object to the form.</p> <p>2 A And it's -- and it's -- I don't know --</p> <p>3 just one comment that it's more detailed, which</p> <p>4 makes someone like me as a third party look at</p> <p>5 and say, well, they actually read the paper. I'd</p> <p>6 worry a little about if reviewer 1 didn't read it</p> <p>7 carefully enough.</p> <p>8 MS. THOMPSON:</p> <p>9 Q But you have no idea what he did?</p> <p>10 A I've been speculating all day.</p> <p>11 Q Okay. All right. And then the first</p> <p>12 sentence of reviewer number 2, "While the authors</p> <p>13 compellingly show changes in several key enzymes</p> <p>14 recognizing redox potential in cells exposed to</p> <p>15 talc, their data do not show, despite the</p> <p>16 author's claim, any evidence that these cells are</p> <p>17 transformed."</p> <p>18 Do you agree with reviewer number 2 in</p> <p>19 that statement?</p> <p>20 A I agree.</p> <p>21 Q Second sentence, "Specifically, no</p> <p>22 experiments documenting changes in cell survival</p> <p>23 proliferation are resistant to apoptosis have</p> <p>24 been performed."</p>
<p style="text-align: right;">Page 343</p> <p>1 Q Yeah.</p> <p>2 A The reviewer's saying it's not</p> <p>3 supported by --</p> <p>4 Q And that's the point I was trying to</p> <p>5 make.</p> <p>6 So -- so you would agree that it</p> <p>7 doesn't sound like it's the statement that's at</p> <p>8 issue; it's whether the talcum powder studies are</p> <p>9 supportive of that statement?</p> <p>10 MS. CURRY:</p> <p>11 Object to the form.</p> <p>12 A Well, the way it's phrased here -- the</p> <p>13 way it's phrased here, I agree. Yeah.</p> <p>14 MS. THOMPSON:</p> <p>15 Q Let's go to reviewer number 2.</p> <p>16 A Uh-huh.</p> <p>17 Q And reviewer number 2 gives a similar</p> <p>18 summary, perhaps with a little more detail.</p> <p>19 A Yeah.</p> <p>20 Q But would you agree it's an accurate</p> <p>21 description of what the objectives of the study</p> <p>22 were?</p> <p>23 A It is.</p> <p>24 MS. CURRY:</p>	<p style="text-align: right;">Page 345</p> <p>1 And that's correct; right?</p> <p>2 A So he does show what he thinks is</p> <p>3 proliferation, if I recall correctly. I believe</p> <p>4 it's an MMT -- MTT assay.</p> <p>5 Q Well, those experiments were done</p> <p>6 following reviewer number 2's recommendation. Is</p> <p>7 that your understanding?</p> <p>8 A Well, I --</p> <p>9 Q In the --</p> <p>10 A Yeah.</p> <p>11 Q In the first manuscript. Do you</p> <p>12 remember that?</p> <p>13 A You could be right. I don't have it</p> <p>14 pre- -- I don't have that version in front of me.</p> <p>15 Q You may have to just take my word for</p> <p>16 that.</p> <p>17 MS. CURRY:</p> <p>18 I have a copy of it if you need it.</p> <p>19 MS. THOMPSON:</p> <p>20 No. It's not too -- I don't think it's</p> <p>21 too much --</p> <p>22 A But I can say, in particular, cell</p> <p>23 survival resistant apoptosis, I don't think has</p> <p>24 been effectively performed.</p>

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<p style="text-align: right;">Page 346</p> <p>1 MS. THOMPSON: 2 Object. That didn't answer a question. 3 Nonresponsive. 4 Q Next sentence, "Consequently, neither 5 tumor initiation nor progression is documented in 6 this study as opposed to the statement in 7 highlight number 1 and elsewhere." 8 "While changes in redox potential play 9 an important role in tumor biology in general, 10 the present data are insufficient to back up the 11 claim that talc is central to the development of 12 ovarian cancer." 13 Did Dr. Saed make a claim that talcum 14 is central to the development of ovarian cancer, 15 that you recall? 16 A I don't recall him saying that. 17 Q I don't either. 18 "Other comments: The introduction 19 should be better organized with shorter 20 description of the general features of ovarian 21 cancer, replaced by a brief overview of redox 22 proteins in cancer, followed by a discussion of 23 their role in ovarian cancer." 24 That's more a style issue. Would you</p>	<p style="text-align: right;">Page 348</p> <p>1 Q Where in -- where in Dr. Saed's paper 2 does it say this paper shows talcum powder 3 transforms ovarian cells? 4 A Do we have the original? 5 Q We're looking at the published 6 manuscript. 7 MS. CURRY: 8 But the comments are based on the -- 9 A This is the one published in -- and you 10 already told me he changed some of the 11 experiments. 12 MS. THOMPSON: 13 Q Was -- shouldn't your critique be the 14 published paper? 15 A Well, you're asking me to review this; 16 right? 17 Q Okay. We can pull out the -- we can 18 pull out the published manuscript. 19 But certainly in the published paper, 20 there are no claims that cells are transformed, 21 are there? 22 A Well, let's take a look. 23 Q It's certainly not in the abstract or 24 in the conclusion -- in the summary, is it?</p>
<p style="text-align: right;">Page 347</p> <p>1 agree? 2 MS. CURRY: 3 Object to the form. 4 A Make it -- make it more readable, yeah. 5 MS. THOMPSON: 6 Q And, then, the -- finally, "The fact 7 that SNPs were changed following such short 8 exposure to talcum is surprising and makes one 9 wonder what the biological effects of such change 10 might be." 11 And those are the reviewer comments 12 from Gynecologic Oncology; correct? 13 A Correct. 14 Q Did the peer-reviewers raise concerns 15 about Dr. Saed's, in your words, unsubstantiated 16 assumptions? 17 A Well, I -- I think it's implicit in 18 some of the comments. 19 Q That there are unsubstantiated 20 assumptions? 21 A So -- so I think if you read the second 22 paragraph of the second reviewer -- remember, 23 this paper basically says that talc transforms 24 ovarian cancer cells.</p>	<p style="text-align: right;">Page 349</p> <p>1 A I'm just getting through the discussion 2 a little bit. It may be -- may be buried in 3 there or may be an implication that the soft 4 argarose cloning is reflective of only the 5 changes. 6 Q Dr. Saed's paper does not claim that 7 the cells were transformed, does it? 8 A Let me look through it, then. 9 Q Okay. Let's go off the record. 10 VIDEOGRAPHER: 11 Off the record at 4:23 p.m. 12 (OFF THE RECORD.) 13 VIDEOGRAPHER: 14 We're back on the record at 4:24 p.m. 15 A Page 7 on the bottom. "In this study 16 we've shown that talc enhances cellular 17 proliferation, induces inhibition of apoptosis 18 and C-cells" -- 19 MS. CURRY: 20 Gotta go slow for Lois. 21 THE WITNESS: 22 Oh. 23 -- "but, more importantly, in normal 24 cells, suggesting talc is a stimulus to the</p>

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<p style="text-align: right;">Page 350</p> <p>1 development of an oncogenic phenotype." 2 MS. THOMPSON: 3 Q That doesn't say the cells were 4 transformed, does it? 5 A I think for those of us in the field 6 that implies transformation. 7 Q Well, it certainly doesn't state -- 8 state cells were transformed, as you stated 9 earlier. 10 MS. CURRY: 11 Object to the form. 12 MS. THOMPSON: 13 Q Did the reviewers have -- raise any 14 concerns about serious flaws in methodology? 15 A You know, the significance of SNP 16 alteration should be further clarified. That's a 17 pleasant way of saying I don't understand what 18 you're doing. 19 Q I'm asking did the peer-reviewers raise 20 concerns about serious flaws in methodology? 21 MS. CURRY: 22 Object to the form. 23 A In those terms? 24 MS. THOMPSON:</p>	<p style="text-align: right;">Page 352</p> <p>1 MS. CURRY: 2 Object to the form. 3 A Correct. 4 MS. THOMPSON: 5 Q And wouldn't that be the flaws in the 6 analysis that you're referring to? 7 A I don't know what that refers to in 8 vis-à-vis my statement. 9 Q Did the reviewers state that any of the 10 cell line findings appeared to be inaccurate? 11 A No. 12 Q Did the reviewers state that the wrong 13 cell lines were used? 14 A No. 15 Q Did the reviewers state that the doses 16 were inappropriate? 17 A No. 18 Q Did the reviewers state that the CA-125 19 findings were irrelevant? 20 MS. CURRY: 21 Object to the form. 22 A Increase in CA-125 while intriguing are 23 not sufficiently convincing to make it relevant 24 or not.</p>
<p style="text-align: right;">Page 351</p> <p>1 Q Yes, in those terms. 2 A No. 3 Q Did the peer-reviewers raise concerns 4 about serious flaws in the experiments? 5 A In those terms? 6 Q Right. 7 A No. 8 Q Did the peer-reviewers raise serious 9 concerns about flaws in the analysis? 10 A No. 11 Q And, in fact, peer-reviewer number 1 12 explicitly stated that "The conclusions are 13 supported by the results." 14 Right? 15 MS. CURRY: 16 Object to the form. 17 A They rejected the paper. 18 MS. THOMPSON: 19 Q I -- that wasn't my question. 20 The question was -- I mean, my question 21 was that the reviewer number 1 specifically 22 states "The conclusions are supported by the 23 results." 24 Correct?</p>	<p style="text-align: right;">Page 353</p> <p>1 MS. THOMPSON: 2 Q But the reviewer certainly didn't say 3 they're irrelevant? 4 A Didn't use those terms. 5 Q And intriguing would at least mean that 6 the reviewer 1 thought they were of some 7 interest. Wouldn't you agree? 8 MS. CURRY: 9 Object to the form. 10 A Some interest. Some interest. 11 MS. THOMPSON: 12 Q The reviewer did ask for clarification 13 of the significance of SNPs. Did the reviewer 14 state that the SNP findings were irrelevant? 15 A Not in those terms. 16 Q Did the reviewer state that the 17 methodology used to test for the SNPs was flawed? 18 A You know, again, they're seeking 19 clarification. That suggests to me that they 20 have a problem with the way it was done. 21 Wouldn't they -- 22 Q Did -- did the reviewer state the 23 methodology used to test the SNPs was flawed? 24 MS. CURRY:</p>

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<p>1 Sorry. You keep cutting off his answer</p> <p>2 when he's not finished.</p> <p>3 MS. THOMPSON:</p> <p>4 Q Were you finished?</p> <p>5 A Well, I'm just asking what are they</p> <p>6 trying to clarify?</p> <p>7 Q I'm just asking you did -- was there a</p> <p>8 comment that the methodology for testing the SNPs</p> <p>9 was flawed?</p> <p>10 MS. CURRY:</p> <p>11 Object to the form.</p> <p>12 A They do not say that.</p> <p>13 MS. THOMPSON:</p> <p>14 Q Okay. Did the reviewers state that the</p> <p>15 SNP data was in a accurate?</p> <p>16 A I don't think they know. It has to be</p> <p>17 clarified.</p> <p>18 Q And are you aware that the same SNP</p> <p>19 data was submitted to SGO as an abstract and</p> <p>20 recently presented at the annual meeting?</p> <p>21 MS. CURRY:</p> <p>22 Object to the form.</p> <p>23 A The one --</p> <p>24 MS. THOMPSON:</p>	<p>1 Q Did the reviewer --</p> <p>2 A I hope not.</p> <p>3 Q Did either reviewer state that the data</p> <p>4 was poor?</p> <p>5 MS. CURRY:</p> <p>6 Object to the form.</p> <p>7 A Not in that specific term.</p> <p>8 MS. THOMPSON:</p> <p>9 Q Let's look at the reviewer from</p> <p>10 Reproductive Sciences.</p> <p>11 Are you going to give me yours?</p> <p>12 A I've got this pretty much memorized.</p> <p>13 MS. EVERETT:</p> <p>14 Did we put it back in the folder? Here</p> <p>15 is one.</p> <p>16 MS. THOMPSON:</p> <p>17 Q Okay. And the paper was accepted at</p> <p>18 Reproductive Sciences. Is that your</p> <p>19 understanding, since it was eventually published?</p> <p>20 A Yes.</p> <p>21 Q Did the reviewers at Reproductive</p> <p>22 Sciences make any statements regarding flawed</p> <p>23 methodology, experiments, or analysis?</p> <p>24 MS. CURRY:</p>
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<p>1 Q As opposed to a presentation?</p> <p>2 A The one in Honolulu -- the one in</p> <p>3 Honolulu --</p> <p>4 Q Yes.</p> <p>5 A -- Hawaii? Yeah. Yes.</p> <p>6 Q Did you see that poster?</p> <p>7 A No.</p> <p>8 Q Did you speak with the -- the authors</p> <p>9 of the abstract and the paper?</p> <p>10 A No.</p> <p>11 Q Would that have been of interest to you</p> <p>12 to -- to speak with the researchers?</p> <p>13 MS. CURRY:</p> <p>14 Object to the form.</p> <p>15 A Yeah. So the poster section conflicted</p> <p>16 with everything else I could do. I didn't see</p> <p>17 any posters. But I think given my role on this,</p> <p>18 I probably would not have gone, under any</p> <p>19 circumstances.</p> <p>20 MS. THOMPSON:</p> <p>21 Q Do you have any knowledge as to whether</p> <p>22 either of these reviewers is a Johnson & Johnson</p> <p>23 consultant or expert?</p> <p>24 A I have no -- no idea.</p>	<p>1 Object to the form.</p> <p>2 A I'm sorry. I only see one reviewer;</p> <p>3 right?</p> <p>4 MS. THOMPSON:</p> <p>5 Q We only have comments from one</p> <p>6 reviewer. That's correct.</p> <p>7 A Yeah. And -- and they don't make that</p> <p>8 comment.</p> <p>9 Q So I want to just go through Dr. Saed's</p> <p>10 published paper --</p> <p>11 A Uh-huh.</p> <p>12 Q -- and discuss what was done in this --</p> <p>13 just from the materials and methods. We're not</p> <p>14 in results yet. Okay?</p> <p>15 So Dr. Saed used the following cell</p> <p>16 lines: SKOV3, A2780, TOV11 -- or 112D. And</p> <p>17 those are all ovarian cancer cell lines; correct?</p> <p>18 A There is significant question about the</p> <p>19 origin of 2780.</p> <p>20 Q Okay.</p> <p>21 A It may --</p> <p>22 Q But it is a cancerous cell line?</p> <p>23 A I would accept that. Yeah.</p> <p>24 Q Okay. And, then, there are also three</p>

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<p style="text-align: right;">Page 358</p> <p>1 noncancerous cell lines. Agree? The human 2 primary normal ovarian epithelial cells from Cell 3 Biologics Chicago, the human ovarian epithelial 4 cells from Cell Biologics, and the human -- oops. 5 A Immortal one. 6 Q And the immortalized human fallopian 7 tube secretory epithelial cells, FT33, from 8 applied biologic materials. 9 Would you agree those are three 10 noncancerous cell lines? 11 A And when you're defining 12 "noncancerous," you mean they were not isolated 13 from a tumor? 14 Q Correct. 15 A Agree on that. 16 Q Again, just going through the 17 methodology, were the cells grown in media and 18 conditions following manufacturer protocol? 19 MS. CURRY: 20 Object to the form. 21 A I'm not really sure what the 22 manufacturer suggested. But I don't -- I think 23 that the way they were cultured appeared okay to 24 me.</p>	<p style="text-align: right;">Page 360</p> <p>1 MS. CURRY: 2 Object to the form. 3 A I believe so. 4 MS. THOMPSON: 5 Q And using the realtime PCR -- RT-PCR, 6 the -- the following assays were performed. Beta 7 actin for normalization of samples; right? 8 A Yes. 9 Q CAT, SOD3? 10 A Uh-huh. 11 Q GSR, GPX1, NOS2. Are those the tests 12 that were performed with PCR? 13 A Seven -- seven genes. 14 Q Yes. 15 A Including beta actin. 16 Q And -- 17 A Yes. 18 Q And by ELISA, Dr. Saed in his lab 19 tested CAT, SOD, GSR, GPX, NPO, and the CA-125 20 that we've talked about before; correct? 21 A Yes. 22 Q And Dr. Saed -- and those have all been 23 peer-reviewed and published in other studies 24 using ELISA and testing those --</p>
<p style="text-align: right;">Page 359</p> <p>1 MS. THOMPSON: 2 Q Appeared what? 3 A Okay to me. 4 Q Okay. And you'll agree that the cells 5 were seeded and treated with zero, 5, 20, or 100 6 micrograms per mil of baby powder; correct? 7 A This is in Treatment of Cells? 8 Q Yes. 9 A Correct. 10 Q And the -- so the talcum powder was 11 dissolved in DMSO; correct? 12 A I am looking for that. Do you see 13 that? 14 Q It's in Treatment of Cells also. 15 A Oh, okay. 16 Q I went out of order. 17 A Thank you. 18 Q And are you aware that these doses have 19 previously been reported in peer-reviewed 20 literature -- 21 MS. CURRY: 22 Object to -- 23 MS. THOMPSON: 24 Q -- for the study of talc?</p>	<p style="text-align: right;">Page 361</p> <p>1 MS. CURRY: 2 Object to the form. 3 A Yes. 4 MS. THOMPSON: 5 Q -- particular markers? 6 And Dr. Saed performed the TaqMan SNP 7 genotyping assay on all cell lines; correct? 8 A It's listed there. Yes. 9 Q And those were performed by the Applied 10 Genomics Technology Center At Wayne State 11 University; correct? 12 A Yes. 13 Q And is it your understanding that this 14 is a core facility? 15 MS. CURRY: 16 Object to the form. 17 A That, I don't know. But it could be. 18 MS. THOMPSON: 19 Q What is a core facility? 20 A It's generally a facility that provides 21 standard assays, and everybody shares, and they 22 charge a fee. 23 Q Is there some accreditation of core 24 facilities for quality control?</p>

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<p style="text-align: right;">Page 362</p> <p>1 A Usually it's institutional. In other</p> <p>2 words, it's not an external group. But a</p> <p>3 institution won't fund the core unless it's doing</p> <p>4 decent work.</p> <p>5 Q And Dr. Saed and his researchers then</p> <p>6 performed the cell proliferation and apoptosis</p> <p>7 studies using the TACS MTT self-proliferation</p> <p>8 assay; correct?</p> <p>9 A Yes.</p> <p>10 Q And -- and cast pace 3 after treatment</p> <p>11 of all the cell lines with the various doses;</p> <p>12 correct?</p> <p>13 A Yes.</p> <p>14 Q And you'll agree that all of these</p> <p>15 tests have been performed, peer-reviewed, and</p> <p>16 published previously by Dr. Saed and others;</p> <p>17 correct?</p> <p>18 MS. CURRY:</p> <p>19 Object to the form.</p> <p>20 A I don't know that. But these are</p> <p>21 reasonably standard.</p> <p>22 MS. THOMPSON:</p> <p>23 Q These are standardized --</p> <p>24 A Yeah.</p>	<p style="text-align: right;">Page 364</p> <p>1 A They're generally accepted. I --</p> <p>2 "standardized" is a difficult word because it</p> <p>3 implies some sort of external review or</p> <p>4 standardization. And that's not true. These are</p> <p>5 kits that are -- are bought and then they're</p> <p>6 implemented in the lab. You still don't know</p> <p>7 whether it's really being done right, but --</p> <p>8 MS. THOMPSON:</p> <p>9 Q Okay. Well it sounds like --</p> <p>10 A -- but -- but -- but they're -- we're</p> <p>11 familiar with these --</p> <p>12 Q Okay.</p> <p>13 A -- and there's nothing too much out of</p> <p>14 the box there.</p> <p>15 Q And before, you said these are</p> <p>16 standardized, yeah, so I was just going back to</p> <p>17 that.</p> <p>18 A Right.</p> <p>19 Q I think we got the answer.</p> <p>20 I'm about to start a little bit</p> <p>21 different area.</p> <p>22 MS. THOMPSON:</p> <p>23 Do we want to take a break now or do</p> <p>24 you want to go for another 30 minutes or so?</p>
<p style="text-align: right;">Page 363</p> <p>1 Q -- testing methods.</p> <p>2 All right. Let -- let me just ask that</p> <p>3 question again because we've got a -- these are</p> <p>4 standardized testing methods; correct?</p> <p>5 MS. CURRY:</p> <p>6 Object to the form.</p> <p>7 A I don't know what you mean by</p> <p>8 "standardized." These are assays that many labs</p> <p>9 use. They're not being done in -- they're not</p> <p>10 being done in a central CLIA-approved lab.</p> <p>11 They're just being done by him and maybe a core</p> <p>12 lab.</p> <p>13 MS. THOMPSON:</p> <p>14 Q And I was just asking the question</p> <p>15 because previously it got chopped into two pieces</p> <p>16 on these are standardized -- yeah, testing</p> <p>17 methods, all right. So I was just trying to get</p> <p>18 a single answer --</p> <p>19 A Yes.</p> <p>20 Q -- was the purpose of that question.</p> <p>21 So these are standardized testing</p> <p>22 methods; correct?</p> <p>23 MS. CURRY:</p> <p>24 Object to the form.</p>	<p style="text-align: right;">Page 365</p> <p>1 MS. CURRY:</p> <p>2 How much time do we have left on the</p> <p>3 record?</p> <p>4 VIDEOGRAPHER:</p> <p>5 An hour and seven minutes.</p> <p>6 MS. CURRY:</p> <p>7 Do you want to take a final break now?</p> <p>8 MS. THOMPSON:</p> <p>9 Yeah. I'll easily finish the rest, I</p> <p>10 think, in an hour and seven minutes.</p> <p>11 MS. CURRY:</p> <p>12 Okay.</p> <p>13 MS. THOMPSON:</p> <p>14 Maybe even less.</p> <p>15 VIDEOGRAPHER:</p> <p>16 Off the record at 4:39 p.m.</p> <p>17 (OFF THE RECORD.)</p> <p>18 VIDEOGRAPHER:</p> <p>19 We're back on the record at 4:50 p.m.</p> <p>20 MS. THOMPSON:</p> <p>21 Q Dr. Birrer, I'd like to do another</p> <p>22 chart with Dr. Saed's research so I can</p> <p>23 understand what your opinions are regarding his</p> <p>24 findings. Okay?</p>

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<p>1 A Okay.</p> <p>2 MS. CURRY:</p> <p>3 And for the record, I object to the</p> <p>4 creation of this chart.</p> <p>5 (DEPOSITION EXHIBIT NUMBER 31 WAS</p> <p>6 MARKED FOR IDENTIFICATION.)</p> <p>7 MS. CURRY:</p> <p>8 What's the exhibit number?</p> <p>9 MS. THOMPSON:</p> <p>10 And this would be Exhibit 31.</p> <p>11 Q And these are the tables taken from</p> <p>12 Dr. Saed's manuscript. Does that look right?</p> <p>13 If you want to compare, you can.</p> <p>14 A Let me just compare.</p> <p>15 MS. CURRY:</p> <p>16 This the from the published manuscript?</p> <p>17 MS. THOMPSON:</p> <p>18 Q This is from the published manuscript?</p> <p>19 A This is from Figure 1, right?</p> <p>20 Q And -- and you'll agree that these</p> <p>21 charts are generated from the raw data; correct?</p> <p>22 MS. CURRY:</p> <p>23 Object to the form.</p> <p>24 A It appears so.</p>	<p>1 MS. CURRY:</p> <p>2 Object to the form.</p> <p>3 A I assume they are. I mean, in terms of</p> <p>4 they reflect the actual raw data, yeah.</p> <p>5 MS. THOMPSON:</p> <p>6 Q Right. So I'm going to put a Y --</p> <p>7 A Okay.</p> <p>8 Q -- for accurate.</p> <p>9 A Oh. You're looking at all of them?</p> <p>10 Q Oh. Do you have any --</p> <p>11 MS. CURRY:</p> <p>12 Do you have the published paper?</p> <p>13 THE WITNESS:</p> <p>14 I have it here. Right here.</p> <p>15 MS. CURRY:</p> <p>16 What exhibit is that?</p> <p>17 THE WITNESS:</p> <p>18 Yeah. Well, I'll have to say, that</p> <p>19 does look different.</p> <p>20 MS. THOMPSON:</p> <p>21 Q I can -- I'll represent that they were</p> <p>22 cut and pasted from the manuscript. So if they</p> <p>23 are different, it's a --</p> <p>24 MS. CURRY:</p>
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<p>1 MS. THOMPSON:</p> <p>2 Q And --</p> <p>3 A Although I would say --</p> <p>4 MS. GARBER:</p> <p>5 Do you have two? Because your</p> <p>6 co-counsel --</p> <p>7 MS. THOMPSON:</p> <p>8 No. That's just one copy, one exhibit.</p> <p>9 A These are -- for instance, the PCR is</p> <p>10 normalized.</p> <p>11 MS. THOMPSON:</p> <p>12 Q Okay. And this chart shows PCR and</p> <p>13 ELISA for antioxidants; right?</p> <p>14 MS. CURRY:</p> <p>15 Object to the form.</p> <p>16 MS. THOMPSON:</p> <p>17 Q The expression of antioxidants and the</p> <p>18 activity of antioxidants CAT and SOV3; correct?</p> <p>19 A Correct.</p> <p>20 Q I want to go through this chart and</p> <p>21 have you tell me "yes" or "no" for each of these</p> <p>22 with each cell line.</p> <p>23 Do you have an opinion as to whether</p> <p>24 these results are accurate?</p>	<p>1 Okay. I'm sorry. I'm having a hard</p> <p>2 time following --</p> <p>3 A But this --</p> <p>4 MS. CURRY:</p> <p>5 -- this because the data represented on</p> <p>6 the exhibit is not reflective of the bar graphs</p> <p>7 that are in the published manuscript.</p> <p>8 So if you can just point us to where in</p> <p>9 the published manuscript you're pulling this</p> <p>10 from.</p> <p>11 MS. THOMPSON:</p> <p>12 All right.</p> <p>13 A This is -- the entire ordinate has</p> <p>14 changed. This is 25. This is 100.</p> <p>15 MS. THOMPSON:</p> <p>16 Q This is -- this is, from the chart,</p> <p>17 this is Figure 1. The color came out a little</p> <p>18 bit differently in the printing process,</p> <p>19 but the --</p> <p>20 MS. CURRY:</p> <p>21 This is not Figure 1.</p> <p>22 A No. Not even close. This is, in fact,</p> <p>23 Figure 3.</p> <p>24 MS. THOMPSON:</p>

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<p style="text-align: right;">Page 370</p> <p>1 Q PCR, CAT, SOD3. CAT activity and SOD</p> <p>2 activity.</p> <p>3 MS. THOMPSON:</p> <p>4 Are y'all looking? Mine are identical.</p> <p>5 Can you be --</p> <p>6 MS. CURRY:</p> <p>7 On the published manuscript, this chart</p> <p>8 does not represent --</p> <p>9 MS. THOMPSON:</p> <p>10 To Figure 1?</p> <p>11 MS. CURRY:</p> <p>12 -- to Figure 1.</p> <p>13 MS. THOMPSON:</p> <p>14 Let's go off the record.</p> <p>15 VIDEOGRAPHER:</p> <p>16 Going off the record at 4:55.</p> <p>17 (OFF THE RECORD.)</p> <p>18 VIDEOGRAPHER:</p> <p>19 We're back on the record at 4:59 p.m.</p> <p>20 MS. THOMPSON:</p> <p>21 Q Okay. Now that we've got that</p> <p>22 straightened out, so you'll agree that this is</p> <p>23 the -- the chart that shows the expression of</p> <p>24 antioxidant CAT and SKOV3 and the activity of the</p>	<p style="text-align: right;">Page 372</p> <p>1 MS. CURRY:</p> <p>2 Object to the form.</p> <p>3 A It could change them considerably,</p> <p>4 yeah.</p> <p>5 MS. THOMPSON:</p> <p>6 Q Do you want to change that to a</p> <p>7 question mark, or do you want to change that to</p> <p>8 no, they're not accurate?</p> <p>9 MS. CURRY:</p> <p>10 Object to the form.</p> <p>11 A Question mark will be fine.</p> <p>12 MS. THOMPSON:</p> <p>13 Q And that would go for all cell lines?</p> <p>14 A Well, the technology -- the techniques</p> <p>15 used was applied to all of them.</p> <p>16 MS. CURRY:</p> <p>17 Just so I know what we're doing here --</p> <p>18 I'm sorry -- is when you're saying results</p> <p>19 accurate in these four pictures, are -- are you</p> <p>20 talking about -- like is that based on raw data</p> <p>21 that's supposed to be in here? I'm just not sure</p> <p>22 what we're doing.</p> <p>23 MS. THOMPSON:</p> <p>24 These graphs are from the raw data.</p>
<p style="text-align: right;">Page 371</p> <p>1 same; correct?</p> <p>2 A You're on Figure 1?</p> <p>3 Q I am on Figure 1, yes.</p> <p>4 A Yeah. That's CAT and SKOV3?</p> <p>5 Q Yeah.</p> <p>6 A Yep.</p> <p>7 Q And we -- we are going through each</p> <p>8 cell line. The first column was Results</p> <p>9 Accurate, and I think --</p> <p>10 A So let me -- let me revise that.</p> <p>11 Q Okay.</p> <p>12 A Because now I understand what we're</p> <p>13 looking at.</p> <p>14 So I think there's a serious problem in</p> <p>15 the PCR, or at least I'd be concerned by that.</p> <p>16 These PCR MRNA levels were normalized to beta</p> <p>17 actin. And I think most of us would accept that</p> <p>18 using one housekeeping gene is not acceptable. I</p> <p>19 would expect at least two or three to make sure</p> <p>20 that there isn't a change in the stability of</p> <p>21 beta actin, which would throw off your</p> <p>22 quantification levels of those genes.</p> <p>23 Q And do you think that would render</p> <p>24 these results inaccurate?</p>	<p style="text-align: right;">Page 373</p> <p>1 MS. CURRY:</p> <p>2 But the raw data, we don't have. That</p> <p>3 hasn't --</p> <p>4 MS. THOMPSON:</p> <p>5 You've seen the raw data in the lab</p> <p>6 notebooks and Dr. Saed has -- is this an</p> <p>7 objection or is this --</p> <p>8 MS. CURRY:</p> <p>9 It's an object- -- I'm just honestly --</p> <p>10 I'm trying -- you're trying to have him create an</p> <p>11 exhibit --</p> <p>12 MS. THOMPSON:</p> <p>13 That's a speaking objection.</p> <p>14 MS. CURRY:</p> <p>15 -- and I'm trying to find out --</p> <p>16 MS. THOMPSON:</p> <p>17 If he understands it, it doesn't really</p> <p>18 matter whether you do or not, Dawn. I mean --</p> <p>19 MS. CURRY:</p> <p>20 And that's fine if you don't want an</p> <p>21 accurate record. That's fine.</p> <p>22 MS. THOMPSON:</p> <p>23 And he hasn't expressed that he doesn't</p> <p>24 understand.</p>

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<p>1 MS. CURRY: 2 That's fine. 3 MS. THOMPSON: 4 Q Dr. Birrer, do you understand what I'm 5 asking with this chart? If not, I'll explain it. 6 A Well, I -- I think -- it's a little bit 7 like the exercise this morning, which is we're 8 creating a document without all the information. 9 I don't have the raw data here. I mean, yeah, 10 it's in the notebooks, I suppose, somewhere. 11 Q And -- and you'll agree that these 12 charts are generated from raw data by a software 13 program. Correct? 14 And Dr. Saed testified to that. 15 Correct? 16 MS. CURRY: 17 Object to the form. 18 A Well, again, depending on what data's 19 put in -- 20 MS. THOMPSON: 21 Q Okay. 22 A -- you could get completely different 23 results. 24 Q I understand. But we're gonna look at</p>	<p>1 A Well, I think the -- if you're gonna 2 call them normal, then the normal primary -- the 3 human primary normal ovarian cell lines would be 4 more relevant. 5 MS. THOMPSON: 6 Q More relevant? But either one would be 7 relevant. Is that what you're saying? 8 MS. CURRY: 9 Object to form. 10 A No. I think the immortalized one is 11 not normal, so it wouldn't be relevant. 12 MS. THOMPSON: 13 Q Okay. So we'll make another column. 14 Well, we don't -- the immortalized and 15 the normal. 16 So the immortalized would be not 17 relevant? 18 A Right. 19 Q And the -- 20 A Yes. 21 Q Maybe I should get a clean -- let's -- 22 let's start over this chart. That's okay. I'll 23 make the next one neater. 24 Okay. Let's start again. And we're</p>
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<p>1 the data that was in the peer-reviewed published 2 paper. Okay? 3 Are the results relevant? And we can 4 go by each cell line. 5 MS. CURRY: 6 Object to the form. 7 MS. THOMPSON: 8 Q And yes or no or you don't know. 9 MS. CURRY: 10 Object to the form. 11 A Well, one of the challenges in this 12 paper is the purpose of the EL1 cell line. I 13 don't think those results are relevant. 14 MS. THOMPSON: 15 Q Okay. The other lines? 16 A The normal ovary, I would assume -- is 17 that primary cells? Right? We reviewed that? 18 Let me go back. 19 So I don't know if that's -- I don't 20 know if that's the HOS cell line or the -- the 21 ones from Cell Biologics. 22 Q Is one relevant and one not? 23 MS. CURRY: 24 Object to the form.</p>	<p>1 gonna distinguish between -- 2 A Uh-huh. 3 Q -- the immortalized, which is IM on the 4 chart, and that's going to be not relevant; 5 right? 6 A Correct. 7 Q And the normal cells are relevant, in 8 your mind? 9 A Uh-huh. 10 Q How about the fallopian tube, the FT33? 11 A Yeah. So that's immortalized also, so 12 I don't think it's particularly relevant. 13 Q Is it not relevant? 14 MS. CURRY: 15 Object to the form. 16 A Uh-huh. 17 MS. THOMPSON: 18 Q And that's because it's immortalized? 19 A Uh-huh. 20 Q Okay. And 3, cancer cell lines? 21 A So this is -- 22 MS. CURRY: 23 Object to the form. 24 A So this was a big -- this was a concern</p>

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<p style="text-align: right;">Page 378</p> <p>1 in the paper, which is that, as you know, SKOV3</p> <p>2 is a clear cell; we've got an endometrioid; and</p> <p>3 we don't even know where 2780 comes from, so I</p> <p>4 don't think they're relevant.</p> <p>5 MS. THOMPSON:</p> <p>6 Q And that's because of lacking a clear</p> <p>7 histologic relationship?</p> <p>8 MS. CURRY:</p> <p>9 Object to the form.</p> <p>10 A That's right.</p> <p>11 MS. THOMPSON:</p> <p>12 Q Do those results show a biological</p> <p>13 effect from talcum powder?</p> <p>14 MS. CURRY:</p> <p>15 Object to the form.</p> <p>16 A So I don't view that -- I don't -- I</p> <p>17 guess the answer is -- biologic effects?</p> <p>18 MS. THOMPSON:</p> <p>19 Q Does something happen when you put the</p> <p>20 baby powder in the cell culture?</p> <p>21 MS. CURRY:</p> <p>22 Object to the form.</p> <p>23 MS. THOMPSON:</p> <p>24 Q This is not related to whether you</p>	<p style="text-align: right;">Page 380</p> <p>1 Q As long as you approve of my work, we</p> <p>2 can -- we can switch the exhibit over to the one</p> <p>3 I'm doing.</p> <p>4 A Uh-huh.</p> <p>5 Q If the results are accurate, do they</p> <p>6 demonstrate a dose-dependent response?</p> <p>7 MS. CURRY:</p> <p>8 I object to the entirety of the</p> <p>9 exercise --</p> <p>10 MS. THOMPSON:</p> <p>11 Okay. You're --</p> <p>12 MS. CURRY:</p> <p>13 -- but I am following you in terms of</p> <p>14 the accuracy of you putting his answers down on</p> <p>15 the paper.</p> <p>16 MS. THOMPSON:</p> <p>17 Okay. All right. And we'll have the</p> <p>18 record, too.</p> <p>19 MS. THOMPSON:</p> <p>20 Q Do the answers show a dose-dependent</p> <p>21 response?</p> <p>22 MS. CURRY:</p> <p>23 Object to the form.</p> <p>24 A So it depends on the cell line, I</p>
<p style="text-align: right;">Page 379</p> <p>1 agree with how it was, the dosage, whether the</p> <p>2 results are accurate or not.</p> <p>3 MS. CURRY:</p> <p>4 Object to the form.</p> <p>5 A Yeah. It's really hard to interpret</p> <p>6 this because, again, I believe he used a control</p> <p>7 with DMSO. DMSO has fairly dramatic effects and</p> <p>8 he's not controlling for it. So, you know, I</p> <p>9 would say no.</p> <p>10 MS. THOMPSON:</p> <p>11 Q No biologic effects?</p> <p>12 A No biologic effects.</p> <p>13 Q On any of the cell lines?</p> <p>14 A Correct. Unless you call PCR effect --</p> <p>15 you know, PCR quantification biologic.</p> <p>16 Q Do you have your exhibit there?</p> <p>17 A Exhibit --</p> <p>18 Q Oh, well. We can -- we'll just use</p> <p>19 mine.</p> <p>20 A This one?</p> <p>21 Q I wondered if you wanted to be filling</p> <p>22 these in yourself. But as long as you correct</p> <p>23 my --</p> <p>24 A You go.</p>	<p style="text-align: right;">Page 381</p> <p>1 think. Right?</p> <p>2 MS. THOMPSON:</p> <p>3 Q Which cell line does not? So --</p> <p>4 MS. CURRY:</p> <p>5 Object to the form.</p> <p>6 A If you look at the PCR, I don't know --</p> <p>7 and you look at everything but EL1, I don't know</p> <p>8 if those are statistically different. If you --</p> <p>9 if you pull it down, you can see it.</p> <p>10 MS. THOMPSON:</p> <p>11 Q Oh, sorry.</p> <p>12 A Yeah. See way on the top?</p> <p>13 Q If the paper says they were</p> <p>14 statistically significant, does that matter?</p> <p>15 MS. CURRY:</p> <p>16 Object to the form.</p> <p>17 A Well, it doesn't look like it to me.</p> <p>18 MS. THOMPSON:</p> <p>19 Q So are you gonna say no or you don't</p> <p>20 know?</p> <p>21 A No.</p> <p>22 MS. CURRY:</p> <p>23 Object to the form.</p> <p>24 MS. THOMPSON:</p>

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<p style="text-align: right;">Page 382</p> <p>1 Q On all cell lines?</p> <p>2 A No. For EL1. Normal ovary.</p> <p>3 So, actually, for -- for -- what is</p> <p>4 that? That's B, SKOV3. So for SKOV3, it looks</p> <p>5 like nothing. It's -- from the mRNA level, it's</p> <p>6 all suppressed. It's all very low. I don't</p> <p>7 see -- I don't see -- if there's a P-value there,</p> <p>8 what is it between? The control and the 5? The</p> <p>9 control and the 20? The 20 and the 100? I don't</p> <p>10 know.</p> <p>11 The ELISA looks like -- this is for</p> <p>12 SKOV3; right? The ELISA looks like there's no</p> <p>13 effect until you get to 20 or 100.</p> <p>14 Q And you're eyeballing the statistical</p> <p>15 significance of these charts?</p> <p>16 A Well, that's why they --</p> <p>17 MS. CURRY:</p> <p>18 Object to the form.</p> <p>19 A That's why they put arrow bars in</p> <p>20 there.</p> <p>21 MS. THOMPSON:</p> <p>22 Q So reading Dr. Saed's results in the</p> <p>23 manuscript --</p> <p>24 A Uh-huh.</p>	<p style="text-align: right;">Page 384</p> <p>1 Q Well, you had the raw data to review,</p> <p>2 didn't you?</p> <p>3 MS. CURRY:</p> <p>4 Object to the form.</p> <p>5 MS. THOMPSON:</p> <p>6 Q It's on your materials considered list.</p> <p>7 A Well, his notebooks were very difficult</p> <p>8 to interpret.</p> <p>9 Q All the raw data was in his notebooks.</p> <p>10 If it -- if you are saying these results were not</p> <p>11 accurate, could you have looked it up in the lab</p> <p>12 notebooks?</p> <p>13 MS. CURRY:</p> <p>14 Object to the form.</p> <p>15 A Yeah, I don't know. I'd have to go</p> <p>16 back and look at it. There were --</p> <p>17 MS. THOMPSON:</p> <p>18 Q Did you do that?</p> <p>19 MS. CURRY:</p> <p>20 Object to the form.</p> <p>21 A I looked at his notebooks. They were</p> <p>22 extremely hard to follow.</p> <p>23 MS. THOMPSON:</p> <p>24 Q Did you ask someone --</p>
<p style="text-align: right;">Page 383</p> <p>1 Q -- the CAT and SKOV -- this is Figure</p> <p>2 1 -- "mRNA and protein levels were significantly</p> <p>3 in a dose-dependent manner in talc-treated cells</p> <p>4 compared to controls."</p> <p>5 Do you disagree with Dr. Saed's</p> <p>6 analysis?</p> <p>7 A I disagree with that statement.</p> <p>8 Q So you're going to say, regardless of</p> <p>9 Dr. Saed's peer-reviewed conclusion, your</p> <p>10 opinion, these do not show a dose-dependent</p> <p>11 response --</p> <p>12 MS. CURRY:</p> <p>13 Object to the form.</p> <p>14 MS. THOMPSON:</p> <p>15 Q -- based on your eyeballing of the</p> <p>16 chart?</p> <p>17 MS. CURRY:</p> <p>18 Object to the form. That's --</p> <p>19 A Well, that -- I disagree with that</p> <p>20 statement. That implies that these are all</p> <p>21 statistically significant, and I can't imagine</p> <p>22 that's true, given the arrow bars. But it would</p> <p>23 be very helpful to have the raw data.</p> <p>24 MS. THOMPSON:</p>	<p style="text-align: right;">Page 385</p> <p>1 MS. CURRY:</p> <p>2 Object to the form.</p> <p>3 MS. THOMPSON:</p> <p>4 Q -- to get information? Because what's</p> <p>5 your evidence that the data wasn't included in</p> <p>6 the lab notebooks?</p> <p>7 MS. CURRY:</p> <p>8 Object to the form.</p> <p>9 A Well, I -- again, his notebooks were</p> <p>10 very poorly organized. There were things that</p> <p>11 were whited out. So it was hard to follow.</p> <p>12 MS. THOMPSON:</p> <p>13 Q Okay. What was whited out? Seriously.</p> <p>14 Was there any data whited out?</p> <p>15 MS. CURRY:</p> <p>16 Object to the form.</p> <p>17 MS. THOMPSON:</p> <p>18 Q You're making --</p> <p>19 A Well, do you have them here?</p> <p>20 MS. THOMPSON:</p> <p>21 Q I do.</p> <p>22 MS. CURRY:</p> <p>23 And the deposition transcript?</p> <p>24 MS. THOMPSON:</p>

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<p>1 I need the lab notebooks. Let's just</p> <p>2 answer this, and I think we're going to move on</p> <p>3 to something else.</p> <p>4 Q In your opinion, are the results</p> <p>5 dose-deponent?</p> <p>6 MS. CURRY:</p> <p>7 Object to the form.</p> <p>8 A So I -- I guess the way to handle that</p> <p>9 would be for -- there looks like there's a dose</p> <p>10 dependency for some of the cell lines in certain</p> <p>11 conditions but not all of them. Is that fair to</p> <p>12 say?</p> <p>13 MS. THOMPSON:</p> <p>14 Q Well, so you don't believe</p> <p>15 Dr. Saed's --</p> <p>16 A Conclusions.</p> <p>17 Q -- conclusions?</p> <p>18 A I don't agree with that one statement.</p> <p>19 His statement is that basically all of the time</p> <p>20 points demonstrated a dose-dependant effect of</p> <p>21 talc. If that's true -- you can't see it here.</p> <p>22 You see it in some.</p> <p>23 Q Did -- did any of the peer-reviewers</p> <p>24 raise a question about that statement?</p>	<p>1 publications using the same methodology and the</p> <p>2 same assays?</p> <p>3 MS. CURRY:</p> <p>4 Object to the form.</p> <p>5 A I didn't -- I didn't go through all of</p> <p>6 his papers, no.</p> <p>7 MS. THOMPSON:</p> <p>8 Q Did you go through any of his previous</p> <p>9 papers?</p> <p>10 MS. CURRY:</p> <p>11 Object to the form.</p> <p>12 A I can't recall going through papers</p> <p>13 that used this technology.</p> <p>14 MS. THOMPSON:</p> <p>15 Q But this technology has been</p> <p>16 peer-reviewed and published --</p> <p>17 MS. CURRY:</p> <p>18 Object to the form.</p> <p>19 A Yes.</p> <p>20 MS. THOMPSON:</p> <p>21 Q -- previously?</p> <p>22 And you're aware that Dr. Saed has</p> <p>23 presented four abstracts based on this research;</p> <p>24 correct?</p>
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<p>1 A No.</p> <p>2 Q And, in fact, the peer-reviewers said</p> <p>3 his conclusions reflected the results; correct?</p> <p>4 MS. CURRY:</p> <p>5 Object to the form.</p> <p>6 MS. THOMPSON:</p> <p>7 Q The peer-reviewer that commented on it?</p> <p>8 A The one reviewer.</p> <p>9 Q The only one that commented on it?</p> <p>10 A Yeah.</p> <p>11 Q So are these question marks or which --</p> <p>12 which cell lines do you think are statistically</p> <p>13 significant?</p> <p>14 A Yeah. I think that's -- I think that's</p> <p>15 probably reasonable, question marks.</p> <p>16 Q Question marks on everything?</p> <p>17 A Yeah.</p> <p>18 Q And there's plenty of discussion for us</p> <p>19 to go back and figure out the reasoning for that.</p> <p>20 We may come back to the chart, but</p> <p>21 there's some other things I want to cover, so</p> <p>22 we'll -- we'll leave that with you disagreeing</p> <p>23 with Dr. Saed's analysis.</p> <p>24 Did you look at Dr. Saed's previous</p>	<p>1 A I believe so.</p> <p>2 Q And abstracts are generally reviewed</p> <p>3 prior to acceptance at a national meeting;</p> <p>4 correct?</p> <p>5 MS. CURRY:</p> <p>6 Object to the form.</p> <p>7 A Usually there's a program committee</p> <p>8 that will review them.</p> <p>9 MS. THOMPSON:</p> <p>10 Q And would you agree that, generally,</p> <p>11 four to six reviewers look at abstracts when</p> <p>12 making the decision which to accept for a</p> <p>13 meeting?</p> <p>14 MS. CURRY:</p> <p>15 Object to the form.</p> <p>16 A It depends on the organization. But</p> <p>17 there usually is -- it's certainly more than one</p> <p>18 person.</p> <p>19 MS. THOMPSON:</p> <p>20 Q If -- if I told you Society For</p> <p>21 Reproductive Investigation typically has four to</p> <p>22 six reviewers and SGO has four to five reviewers</p> <p>23 for each abstract, does that sound reasonable?</p> <p>24 MS. CURRY:</p>

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<p>1 Object to the form.</p> <p>2 A You know, I think for the first</p> <p>3 society, the former one, I'm not familiar with</p> <p>4 them, but it sounds reasonable.</p> <p>5 SGO, I've been on the program</p> <p>6 committee. Sometimes it's a little less than</p> <p>7 that depending on how many abstracts you get.</p> <p>8 MS. THOMPSON:</p> <p>9 Q At least for this year, there were four</p> <p>10 to five reviewers, and the abstracts were scored</p> <p>11 numerically.</p> <p>12 Are you familiar with that system?</p> <p>13 MS. CURRY:</p> <p>14 Object to the form.</p> <p>15 A I am.</p> <p>16 MS. THOMPSON:</p> <p>17 Q And the -- and the top scoring</p> <p>18 abstracts were accepted for presentation?</p> <p>19 A Usually they'll put a cutoff on it,</p> <p>20 yeah.</p> <p>21 Q And in the two criteria that SGO</p> <p>22 reviewers looked at were, one, scientific</p> <p>23 validity; and two, clinical relevance.</p> <p>24 Does that sound right?</p>	<p>1 You would agree with me that there have</p> <p>2 been at least 20 to 30 eyes on this research;</p> <p>3 correct?</p> <p>4 MS. CURRY:</p> <p>5 Object to the form.</p> <p>6 MS. THOMPSON:</p> <p>7 Q In various levels of review.</p> <p>8 MS. CURRY:</p> <p>9 Object to the form.</p> <p>10 A 20 to 30 sounds a little excessive but</p> <p>11 probably --</p> <p>12 MS. THOMPSON:</p> <p>13 Q Well, four abstracts, four to five</p> <p>14 reviewers each --</p> <p>15 A Oh, you're saying all of it?</p> <p>16 Q Yeah. Combined.</p> <p>17 MS. CURRY:</p> <p>18 Objection.</p> <p>19 MS. THOMPSON:</p> <p>20 Q Would you agree that there have been at</p> <p>21 least 25 eyes on this research?</p> <p>22 A Uh-huh. Some could have overlapped.</p> <p>23 MS. GARBER:</p> <p>24 Or 50 eyes, since there's two.</p>
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<p>1 MS. CURRY:</p> <p>2 Object to the form.</p> <p>3 A That, I don't know.</p> <p>4 MS. THOMPSON:</p> <p>5 Q And -- and you'll agree that the</p> <p>6 mutation, the SNP data, was presented as a poster</p> <p>7 at this year's SGO meeting; correct?</p> <p>8 MS. CURRY:</p> <p>9 Object to the form.</p> <p>10 A I didn't -- I didn't go to that poster,</p> <p>11 so I don't know what was on it. If it was a --</p> <p>12 if it was similar to the paper, I would assume</p> <p>13 so.</p> <p>14 MS. THOMPSON:</p> <p>15 Q Okay. So if you have the manuscript</p> <p>16 that was reviewed by at least two reviewers and</p> <p>17 the editors of Gynecologic Oncology, you have the</p> <p>18 manuscript that was reviewed by at least one</p> <p>19 editor -- one reviewer and editor for</p> <p>20 Reproductive Sciences. You have abstracts that</p> <p>21 are each reviewed by four to five reviewers. He</p> <p>22 also has a book chapter that was reviewed,</p> <p>23 peer-reviewed by editors which included this</p> <p>24 data.</p>	<p>1 MS. THOMPSON:</p> <p>2 Q Fifty eyes.</p> <p>3 Are you aware of any other reviewers</p> <p>4 that raised the serious concerns that you seem to</p> <p>5 have with Dr. Saed's paper --</p> <p>6 MS. CURRY:</p> <p>7 Object to the form.</p> <p>8 MS. THOMPSON:</p> <p>9 Q -- and -- and research?</p> <p>10 A I don't know any of the reviewers for</p> <p>11 the abstracts or the SGO. That's all kept</p> <p>12 confidential. So none of them have -- I haven't</p> <p>13 any firsthand knowledge that they said to me.</p> <p>14 But the review process hasn't raised -- hasn't</p> <p>15 necessarily raised the issues that I've raised.</p> <p>16 Q Okay.</p> <p>17 A But that doesn't change my opinion.</p> <p>18 Q I didn't ask you, actually. If it did,</p> <p>19 I didn't expect it to.</p> <p>20 I want to go through -- oh.</p> <p>21 (DEPOSITION EXHIBIT NUMBER 32 WAS</p> <p>22 MARKED FOR IDENTIFICATION.)</p> <p>23 MS. THOMPSON:</p> <p>24 Q And did you -- did you review</p>

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<p>1 Dr. Saed's review article published in 2 Gynecologic Oncology in 2017? 3 A I think I saw this. Is this on 4 oxidative stress? 5 Q Yes. 6 A Yeah. Yeah. 7 Q And -- and do you know if this review 8 article was invited or submitted and 9 peer-reviewed in the process? 10 A I don't know. 11 Q But, as you've testified before, and 12 typically authors of review articles in reputable 13 journals are felt to be experts in the field; 14 correct? 15 MS. CURRY: 16 Object to the form. 17 A They generally are. 18 MS. THOMPSON: 19 Q And -- 20 MS. CURRY: 21 Did you mark this as an exhibit? 22 MS. EVERETT: 23 It's Exhibit 32. 24 MS. THOMPSON:</p>	<p>1 MS. THOMPSON: 2 Q Yes. 3 A It's not the same phrase. Essential 4 role -- actually, the essential role here is 5 pretty narrow. But it -- but, you know, I 6 wouldn't quibble about that. It's in the same 7 range. 8 Q It's a similar concept that's -- that 9 was published in the review article; correct? 10 A Uh-huh. 11 MS. CURRY: 12 Object to the form. 13 MS. THOMPSON: 14 Q Reading the abstract "Clinical and 15 epidemiological investigations have provided 16 evidence supporting the role of reactive oxygen 17 species, ROS, and reactive nitrogen species, RNS, 18 collectively known as oxidative stress in the 19 etiology of cancer." 20 Would you agree with that statement? 21 MS. CURRY: 22 Object to the form. 23 A Yep. 24 MS. THOMPSON:</p>
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<p>1 32. 2 MS. CURRY: 3 Okay. Thank you. 4 MS. THOMPSON: 5 Q And just looking at the abstract on -- 6 well, first on the highlights -- this review 7 article updates the role of oxidative stress and 8 the pathogenesis of ovarian cancer. 9 The first highlight is "Oxidative 10 Stress Plays an Essential Role in the 11 Pathogenesis of Ovarian Cancer." 12 A Where are you? I'm sorry. 13 Q The highlights at the top. 14 A Oh. The bullet points? 15 Q Bullet point, highlights. 16 A Okay. 17 Q And you'll agree that -- that statement 18 is essentially the same as the one in the talcum 19 powder article that was asked to be removed 20 because of the data not supporting that 21 statement; correct? 22 MS. CURRY: 23 Object to the form. 24 A You're going on submission?</p>	<p>1 Q "Exogenous factors such as chronic 2 inflammation, infection and hypoxia are major 3 sources of cellular oxidative stress." 4 Would you agree with that statement? 5 MS. CURRY: 6 Object to the form. 7 A Well, I would just refine it to say 8 they were sources. I don't know if they're the 9 major sources. In certain conditions there may 10 be other sources. So it's a little bit of a 11 generality. 12 MS. THOMPSON: 13 Q "Specifically oxidative stress plays an 14 important role in the pathogenesis, 15 neoangiogenesis and dissemination of local or 16 distant ovarian cancer, as it is known to induce 17 phenotypic modifications of tumor cells by 18 crosstalk between tumor cells and the surrounding 19 stroma." 20 Do you agree with that statement? 21 A Well, that's a mouthful. There's a lot 22 in there, and I'm not so sure I know exactly what 23 he's talking about. Pathogenesis is pretty 24 general. Blood vessel formation is a different</p>

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<p style="text-align: right;">Page 398</p> <p>1 process. So --</p> <p>2 Q But certainly the reviewers and the</p> <p>3 editors of the journal, when they published the</p> <p>4 review article --</p> <p>5 A Uh-huh.</p> <p>6 Q -- thought that was accurate</p> <p>7 information; correct?</p> <p>8 A They did.</p> <p>9 MS. CURRY:</p> <p>10 Object to the form.</p> <p>11 A Yeah.</p> <p>12 MS. THOMPSON:</p> <p>13 Q Going to Table 1 on page 598, that's a</p> <p>14 "Summary of the Oxidant and Antioxidant</p> <p>15 Expression and Sensitive and Chemoresistant</p> <p>16 Ovarian Cancer." You'll agree that these were</p> <p>17 essentially the same markers that Dr. Saed</p> <p>18 studied in the talcum powder experiments;</p> <p>19 correct?</p> <p>20 MS. CURRY:</p> <p>21 Object to the form.</p> <p>22 MS. THOMPSON:</p> <p>23 Q NPO, INOS?</p> <p>24 A I think so. I think so. I'm just</p>	<p style="text-align: right;">Page 400</p> <p>1 MS. THOMPSON:</p> <p>2 Q But the -- but the markers are the</p> <p>3 same, essentially?</p> <p>4 MS. CURRY:</p> <p>5 Object to the form.</p> <p>6 A The markers are the same.</p> <p>7 MS. THOMPSON:</p> <p>8 Q And they're published in this review</p> <p>9 article, correct, in Gynecologic Oncology?</p> <p>10 A They're reported here and published.</p> <p>11 Q And you'll agree there have been some</p> <p>12 other molecular studies relating to talcum powder</p> <p>13 and cell culture; correct?</p> <p>14 MS. CURRY:</p> <p>15 Object to the form.</p> <p>16 A I believe so.</p> <p>17 MS. THOMPSON:</p> <p>18 Q Are you familiar with a Shukla paper?</p> <p>19 A Yes, I am.</p> <p>20 Q I'll mark the Shukla paper Exhibit 33.</p> <p>21 (DEPOSITION EXHIBIT NUMBER 33 WAS</p> <p>22 MARKED FOR IDENTIFICATION.)</p> <p>23 MS. THOMPSON:</p> <p>24 Q Okay. And this paper was published in</p>
<p style="text-align: right;">Page 399</p> <p>1 checking all of them. Did they --</p> <p>2 Q And generally speaking.</p> <p>3 A Certainly the lower list is all in</p> <p>4 there, yeah.</p> <p>5 Q So -- so these -- these oxidants,</p> <p>6 antioxidants that Dr. Saed studied with the</p> <p>7 talcum powder, he had published before; correct?</p> <p>8 MS. CURRY:</p> <p>9 Object to the form.</p> <p>10 A Well, this is a review article. He's</p> <p>11 not publishing primary data right now. He's just</p> <p>12 noting it.</p> <p>13 MS. THOMPSON:</p> <p>14 Q A review article noting the relevance</p> <p>15 of those assays for oxidative stress in ovarian</p> <p>16 cancer; correct?</p> <p>17 MS. CURRY:</p> <p>18 Object to the form.</p> <p>19 A Well, again, I'm refining that a little</p> <p>20 bit because this table really looks for</p> <p>21 expression comparing standard ovarian cancer to</p> <p>22 chemoresistance. That's really not what this</p> <p>23 paper is about. So it's kind of apples and</p> <p>24 oranges.</p>	<p style="text-align: right;">Page 401</p> <p>1 2008; correct?</p> <p>2 MS. CURRY:</p> <p>3 Object to the form.</p> <p>4 MS. THOMPSON:</p> <p>5 Q Sorry. Received in --</p> <p>6 A That was in '9.</p> <p>7 Q In formal form, 2008.</p> <p>8 MS. CURRY:</p> <p>9 Do you have a copy?</p> <p>10 A This is in 2009, I have it.</p> <p>11 MS. THOMPSON:</p> <p>12 Q The title is "Alterations in Gene</p> <p>13 Expression in Human Mesothelia Cells Correlate</p> <p>14 with Mineral Pathogenicity."</p> <p>15 Is that the title of this paper that</p> <p>16 you have?</p> <p>17 A Yes. Yes.</p> <p>18 Q Okay. And it was published in --</p> <p>19 A I have it 2009.</p> <p>20 Q Oh. No. We're looking at -- I'm</p> <p>21 looking at that received in final form, and</p> <p>22 you're -- when it actually appeared. You're</p> <p>23 correct. 2009.</p> <p>24 And this paper looked at cell culture</p>

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<p style="text-align: right;">Page 402</p> <p>1 with asbestos applied; correct?</p> <p>2 A This looked at asbestos, nonfibrous</p> <p>3 talc, and titanium dioxide.</p> <p>4 Q Correct.</p> <p>5 A Or glass beads.</p> <p>6 Q And if you'll turn to Table 2, it</p> <p>7 reports on gene expression and mesothelial cells</p> <p>8 at low and high doses at 8 and 24 hours for the</p> <p>9 low dose and 8 hours for the high dose. Correct?</p> <p>10 A This is genes that are affected by</p> <p>11 asbestos.</p> <p>12 Q Correct.</p> <p>13 And, then, if you'll look at table --</p> <p>14 A And this -- sorry.</p> <p>15 Q -- Table 3, which are the genes</p> <p>16 upregulated by nonfibrous talc, you'll see that</p> <p>17 testing was done at 8 hours at low and high dose.</p> <p>18 And it appears that there was no testing done at</p> <p>19 24 hours for talc.</p> <p>20 Is that your understanding?</p> <p>21 A I believe so.</p> <p>22 Q And, yet, there --</p> <p>23 A I'm sorry. Can I refine that?</p> <p>24 MS. CURRY:</p>	<p style="text-align: right;">Page 404</p> <p>1 Q Yeah, ATF.</p> <p>2 And those are cancer genes; correct?</p> <p>3 Or genes affiliated -- associated with cancer?</p> <p>4 MS. CURRY:</p> <p>5 Object to the form.</p> <p>6 A Well, a lot of genes are.</p> <p>7 ATF3 --</p> <p>8 MS. THOMPSON:</p> <p>9 Q ATF3 and interleukin 8 are often</p> <p>10 studied in relationship to cancer association;</p> <p>11 correct?</p> <p>12 MS. CURRY:</p> <p>13 Object to the form.</p> <p>14 A I'd say interleukin 8. I don't -- I</p> <p>15 know of less data for ATF3. It's a transcription</p> <p>16 factor, so I don't know the story there.</p> <p>17 But your original question, these are</p> <p>18 statistically significant increases at 8 hours</p> <p>19 for talc; right?</p> <p>20 MS. THOMPSON:</p> <p>21 Q And 24 hours for talc was not</p> <p>22 performed; correct?</p> <p>23 MS. CURRY:</p> <p>24 Object to the form.</p>
<p style="text-align: right;">Page 403</p> <p>1 Object to the form. Sorry.</p> <p>2 A They were -- it was checked but the</p> <p>3 changes were not observed.</p> <p>4 MS. THOMPSON:</p> <p>5 Q Where do you see that?</p> <p>6 A Well, that may be -- hang on. "These</p> <p>7 are mesothelial cells..." Yeah. Right --</p> <p>8 assuming I'm reading this right.</p> <p>9 Right below the table it says "...were</p> <p>10 initially -- were observed initially with talc at</p> <p>11 8 hours. However, these changes were not</p> <p>12 observed at 24 hours. Suggesting that the human</p> <p>13 mesothelial cells adapt to this mineral."</p> <p>14 Q If you'll look at Table -- at Figure</p> <p>15 4 --</p> <p>16 A Figure 4.</p> <p>17 Q -- you do see that there are</p> <p>18 significant increases in both nonfibrous talc and</p> <p>19 the crocidolite asbestos; correct?</p> <p>20 MS. CURRY:</p> <p>21 Object to the form.</p> <p>22 A So this is quantitative PCR of two</p> <p>23 genes; right? This is ATF3?</p> <p>24 MS. THOMPSON:</p>	<p style="text-align: right;">Page 405</p> <p>1 A It was performed but they didn't see</p> <p>2 any changes.</p> <p>3 MS. THOMPSON:</p> <p>4 Q Was it performed at the high dose?</p> <p>5 A Well, let's see. I can't answer that.</p> <p>6 It may be buried in here somewhere. I do -- I do</p> <p>7 note that in this paper they didn't detect a lot</p> <p>8 of gene changes with talc.</p> <p>9 Q They did detect gene changes with talc,</p> <p>10 did they not?</p> <p>11 MS. CURRY:</p> <p>12 Object to the form.</p> <p>13 A Well, they didn't detect a lot. There</p> <p>14 were some.</p> <p>15 MS. THOMPSON:</p> <p>16 Q I didn't ask if there were a lot.</p> <p>17 There were gene changes with talc?</p> <p>18 A Uh-huh.</p> <p>19 Q Would you consider that a biological</p> <p>20 effect?</p> <p>21 MS. CURRY:</p> <p>22 Object to the form.</p> <p>23 A So, I -- yeah. I don't consider it</p> <p>24 biologic. It may be transcriptional.</p>

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<p style="text-align: right;">Page 406</p> <p>1 MS. THOMPSON: 2 Q And you've looked at the Buz'Zard 3 paper; correct? The Pycnogenol paper, does that 4 sound familiar? 5 A Well, I don't recognize that name. 6 Yeah. I did look at it. 7 Q Okay. I'm gonna mark that as Exhibit 8 34. 9 (DEPOSITION EXHIBIT NUMBER 34 WAS 10 MARKED FOR IDENTIFICATION.) 11 MS. THOMPSON: 12 Q And you'll agree that this paper looked 13 at neoplastic transformation in humans' ovarian 14 cell cultures exposed to talc; correct? 15 A Well, this gets back to what we 16 discussed before. I think they -- they -- the 17 title says it and they -- and they argue that 18 what they've shown is transformation. I don't -- 19 I don't agree with that. 20 Q Well, at least the authors say that, in 21 reading from the abstract, two-thirds of the way 22 down, "Talc increased proliferation, induced 23 neoplastic transformation and increased ROS 24 generation timed dependently in the ovarian cells</p>	<p style="text-align: right;">Page 408</p> <p>1 think about Buz'Zard. I'd have to cross-compare 2 that. 3 MS. THOMPSON: 4 Q Well, I'm just asking you if it refutes 5 his findings. 6 MS. CURRY: 7 Object to the form. 8 A No. I -- I'm thinking about that. I 9 think his ROS generation is a little bit 10 different, Buz'Zard. 11 MS. THOMPSON: 12 Q The ROS generation may be a little bit 13 different, but it does show ROS generation in 14 that paper; correct? 15 MS. CURRY: 16 Object to the form. 17 A Now, the Buz'Zard was -- was, for lack 18 of a better term, bizarre, because there were 19 differential effects in terms of production of 20 ROS depending on the concentration. So I found 21 it very difficult. And the interpretation that 22 they had was, I thought, misleading. 23 MS. THOMPSON: 24 Q But the question was: Did it in any</p>
<p style="text-align: right;">Page 407</p> <p>1 and dosed dependently in the p.m." 2 And that's at least what the authors 3 conclude; right? 4 A That's what they say in the abstract, 5 yes. 6 Q And also conclude that "The data 7 suggests that talc may contribute to ovarian 8 neoplastic transformation" -- 9 A Where are you now? I'm sorry. The 10 next sentence? 11 Q Next-to-last sentence. 12 A Yep. 13 Q "The data suggests that talc may 14 contribute to ovarian neoplastic transformation 15 and Pyc reduced the talc-induced transformation." 16 That's what the authors concluded; 17 correct? 18 A That's what they say. 19 Q Do either the Shukla paper or the 20 Buz'Zard paper refute Dr. Saed's research 21 findings? 22 MS. CURRY: 23 Object to the form. 24 A I don't think Shukla does. I'd have to</p>	<p style="text-align: right;">Page 409</p> <p>1 way refute Dr. Saed's findings? 2 MS. CURRY: 3 Object to the form. 4 A In -- in terms of comparing this to 5 that? 6 MS. THOMPSON: 7 Q Yes. 8 A I'd have to take a close look at that. 9 It's not something I thought about. 10 Q Okay. But there's nothing that's 11 obvious that refutes Dr. Saed's -- 12 A It's not leaping out to me. 13 (DEPOSITION EXHIBIT NUMBER 35 WAS 14 MARKED FOR IDENTIFICATION.) 15 MS. THOMPSON: 16 Q Okay. I'm marking as Exhibit 35 a 17 paper by Akhtar from 2010. 18 Have you seen this paper? 19 A This one, I don't think I reviewed. 20 Let me just see if it's on my list. No. 21 Q And are you aware from Dr. Saed's 22 deposition that he referred to the -- this paper 23 to establish his dosages for the talc experiments 24 that Dr. Saed performed?</p>

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<p>1 A In terms of what he did?</p> <p>2 Q Yes.</p> <p>3 A No, I didn't. I'm not aware of that</p> <p>4 from his deposition.</p> <p>5 Q Looking at the paper --</p> <p>6 A Yeah.</p> <p>7 Q -- does that look reasonable?</p> <p>8 MS. CURRY:</p> <p>9 Object to the form.</p> <p>10 A This is way out of my purview with iron</p> <p>11 mediated lipid peroxidase in A459 cells, which</p> <p>12 are lung cancer. I don't know the relevance of</p> <p>13 this to what we're addressing here.</p> <p>14 MS. THOMPSON:</p> <p>15 Q Well, let's read what he says --</p> <p>16 A Sure.</p> <p>17 Q -- in the abstract.</p> <p>18 "Talc particles, the basic ingredient</p> <p>19 in different kinds of talc-based cosmetic and</p> <p>20 pharmaceutical products pose a health risk to</p> <p>21 pulmonary and ovarian systems due to domestic and</p> <p>22 occupational exposures."</p> <p>23 Is that what the authors say?</p> <p>24 A Correct.</p>	<p>1 MS. THOMPSON:</p> <p>2 Q Well, it's the first statement of the</p> <p>3 abstract.</p> <p>4 A Right.</p> <p>5 Q Do you think that's just an irrelevant</p> <p>6 statement, that they put as the first -- the</p> <p>7 introductory sentence to their paper?</p> <p>8 MS. CURRY:</p> <p>9 Object to the form.</p> <p>10 A Well, I think that's their supposition.</p> <p>11 They make that statement. I get it. But that</p> <p>12 doesn't mean that this experiment is relevant to</p> <p>13 that.</p> <p>14 MS. THOMPSON:</p> <p>15 Q I'm asking do the authors think it was</p> <p>16 relevant?</p> <p>17 MS. CURRY:</p> <p>18 Object to the form.</p> <p>19 A You'd have to address it with them. I</p> <p>20 don't know.</p> <p>21 MS. THOMPSON:</p> <p>22 Q "The talc particles, the basic</p> <p>23 ingredient in different kinds of talc-based</p> <p>24 cosmetic and pharmaceutical products pose a</p>
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<p>1 Q So at least the authors thought that</p> <p>2 this experiment had relevance to talc-based</p> <p>3 cosmetic products; correct?</p> <p>4 MS. CURRY:</p> <p>5 Object to the form.</p> <p>6 A Yeah. I think it's in that sentence.</p> <p>7 MS. THOMPSON:</p> <p>8 Q And at least the authors thought that</p> <p>9 these experiments had relevance to the ovarian</p> <p>10 system; correct?</p> <p>11 MS. CURRY:</p> <p>12 Object to the form.</p> <p>13 A Well, they mentioned it. And as a -- I</p> <p>14 think as a premise to the experiment. That</p> <p>15 doesn't mean it's relevant.</p> <p>16 MS. THOMPSON:</p> <p>17 Q Well, it's a -- you would assume that</p> <p>18 if it's a premise to do the experiment, that they</p> <p>19 thought the experiments would be relevant to the</p> <p>20 question that they're asking; correct?</p> <p>21 MS. CURRY:</p> <p>22 Object to the form.</p> <p>23 A There's no question there. That's a</p> <p>24 statement. It's in the --</p>	<p>1 health risk to pulmonary and ovarian systems due</p> <p>2 to domestic and occupational exposure."</p> <p>3 And then they go on to why they're</p> <p>4 studying talc particles.</p> <p>5 Is -- is it your testimony that you</p> <p>6 don't know whether the authors thought that was</p> <p>7 relevant or not?</p> <p>8 MS. CURRY:</p> <p>9 Object to the form.</p> <p>10 A Well, it's speculation. I don't know</p> <p>11 what was in their mind. I can read this. I see</p> <p>12 what they did. And that opening statement is,</p> <p>13 again, sort of setting the -- setting the plate.</p> <p>14 But is this system relevant to that? I don't</p> <p>15 know. Lipid peroxidation --</p> <p>16 MS. THOMPSON:</p> <p>17 Q But -- but you would agree that the</p> <p>18 peer-reviewers and the editors of this journal</p> <p>19 accepted this paper with the introduction that</p> <p>20 talc particles posed a risk to pulmonary and</p> <p>21 ovarian systems and that the investigators at</p> <p>22 least did the experiments and published the</p> <p>23 paper; correct?</p> <p>24 MS. CURRY:</p>

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<p style="text-align: right;">Page 414</p> <p>1 Object to the form.</p> <p>2 A Did the work and published the paper.</p> <p>3 Agree.</p> <p>4 MS. THOMPSON:</p> <p>5 Q And in the conclusion, the authors</p> <p>6 state "We have presented a preliminary data on</p> <p>7 the toxicity response elicited by the two types</p> <p>8 of talc nano particles depending on their</p> <p>9 different geologic origin," and then go on to</p> <p>10 conclude, the end, "Data clearly suggests that</p> <p>11 exposure to talc, particularly nanopowder, should</p> <p>12 be protected in humans at risk of occupational as</p> <p>13 well as domestic exposure."</p> <p>14 That's the conclusions of the authors</p> <p>15 based on this research; correct?</p> <p>16 A That's the last sentence? Is that the</p> <p>17 last sentence?</p> <p>18 Q Yes.</p> <p>19 A Yeah. That's what they say.</p> <p>20 Q That is in the conclusion?</p> <p>21 A That's what they say.</p> <p>22 Q And that is the "Conclusion" section of</p> <p>23 the paper; correct?</p> <p>24 A Correct.</p>	<p style="text-align: right;">Page 416</p> <p>1 Object to the form.</p> <p>2 A Well, I just saw it. I haven't</p> <p>3 reviewed it. I would be concerned that they're</p> <p>4 in a completely different cell system. And, as</p> <p>5 you know, there's just huge differences in tissue</p> <p>6 responses.</p> <p>7 MS. THOMPSON:</p> <p>8 Q Would that automatically make it</p> <p>9 irrelevant, in your mind?</p> <p>10 MS. CURRY:</p> <p>11 Object to the form.</p> <p>12 A I would -- I'd like to read the paper.</p> <p>13 But I'd be concerned. I would start out with a</p> <p>14 certain concern about that and then go through</p> <p>15 the paper.</p> <p>16 MS. THOMPSON:</p> <p>17 Q Okay. We can go off the record, and</p> <p>18 you -- you can look at the paper.</p> <p>19 A Okay.</p> <p>20 VIDEOGRAPHER:</p> <p>21 Off the record at 5:38 p.m.</p> <p>22 (OFF THE RECORD.)</p> <p>23 VIDEOGRAPHER:</p> <p>24 We're back on the record at 5:40 p.m.</p>
<p style="text-align: right;">Page 415</p> <p>1 (DEPOSITION EXHIBIT NUMBER 36 WAS</p> <p>2 MARKED FOR IDENTIFICATION.)</p> <p>3 MS. THOMPSON:</p> <p>4 Q I'm marking as Exhibit 36 another paper</p> <p>5 by Akhtar and colleagues published in 2012.</p> <p>6 Have you seen that paper, Dr. Birrer?</p> <p>7 A No.</p> <p>8 Q This paper is titled "Cytotoxicity and</p> <p>9 Apoptosis" --</p> <p>10 MS. CURRY:</p> <p>11 Do you have a copy? Sorry.</p> <p>12 MS. THOMPSON:</p> <p>13 I'm sorry.</p> <p>14 MS. CURRY:</p> <p>15 Thank you.</p> <p>16 MS. THOMPSON:</p> <p>17 Q This paper is titled "Cytotoxicity and</p> <p>18 Apoptosis Induction by Nano-Scale Talc Particles</p> <p>19 From Two Different Geographical Regions in Human</p> <p>20 Lung Epithelial Cells."</p> <p>21 Is it your opinion that this paper is</p> <p>22 irrelevant because it tested the biological</p> <p>23 effects of talc in human lung epithelial cells?</p> <p>24 MS. CURRY:</p>	<p style="text-align: right;">Page 417</p> <p>1 MS. THOMPSON:</p> <p>2 Q Dr. Birrer, this article titled</p> <p>3 "Cytotoxicity and Apoptosis Induction by</p> <p>4 Nano-Scale Talc Particles from Two Different</p> <p>5 Geographical Regions in Human Lung Epithelial</p> <p>6 Cells" is by the same authors of the paper we</p> <p>7 just discussed; right?</p> <p>8 A Correct. I don't know if they're all</p> <p>9 on here, but it's the same group.</p> <p>10 Q Same group.</p> <p>11 A Yeah.</p> <p>12 Q Going to the last sentence on the first</p> <p>13 page in the introduction, the authors state:</p> <p>14 "Epidemiologic evidence also suggest a possible</p> <p>15 association between genital use of talcum powder</p> <p>16 and risk of ovarian cancer. Talc also appears to</p> <p>17 induce reactive oxygen, ROS, generation,</p> <p>18 oxidative stress, and inflammation."</p> <p>19 Is that what the authors state</p> <p>20 regarding the epidemiology of talcum powder and a</p> <p>21 reason for studying the cellular response?</p> <p>22 MS. CURRY:</p> <p>23 Object to the form.</p> <p>24 A So the first statement is about</p>

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<p style="text-align: right;">Page 418</p> <p>1 epidemiologic evidence. The second statement is</p> <p>2 about reactive oxygen species. And they don't</p> <p>3 say anything about why there's a reason to study.</p> <p>4 They just make those statements.</p> <p>5 MS. THOMPSON:</p> <p>6 Q Is it your testimony that they would</p> <p>7 just put -- put that statement in randomly in the</p> <p>8 introduction to their paper about cytotoxicity and</p> <p>9 apoptosis with talc particles?</p> <p>10 MS. CURRY:</p> <p>11 Object to the form.</p> <p>12 A It wouldn't be random. But, again, I</p> <p>13 think it's just a piece of information that this</p> <p>14 has been studied before in a different system.</p> <p>15 MS. THOMPSON:</p> <p>16 Q And you would -- and they cite to</p> <p>17 Buz'Zard, the paper we just reviewed; correct?</p> <p>18 A Uh-huh. Yes.</p> <p>19 Q And they start -- cite to Langseth;</p> <p>20 correct?</p> <p>21 A Yes.</p> <p>22 Q And in previous testimony you have</p> <p>23 testified that you think that Langseth is a -- is</p> <p>24 a high-quality paper. Do you remember that?</p>	<p style="text-align: right;">Page 420</p> <p>1 Is that what the authors conclude from</p> <p>2 the experiments that they did on nano talc</p> <p>3 particles?</p> <p>4 A That's what they say right there, yeah.</p> <p>5 Q And we've established earlier that the</p> <p>6 baby powder is a mixed particle-sized product;</p> <p>7 correct?</p> <p>8 MS. CURRY:</p> <p>9 Object to the form.</p> <p>10 A Well, we talked about talc particles,</p> <p>11 and I simply said my understanding is not as a</p> <p>12 mineralogist, but my understanding is a different</p> <p>13 spectrum. I don't --</p> <p>14 MS. THOMPSON:</p> <p>15 Q And do you know one way or the other</p> <p>16 whether some of the particles in baby powder</p> <p>17 could be classified as nano particles?</p> <p>18 A No, I don't know that.</p> <p>19 Q Do either of the Akhtar papers that we</p> <p>20 just looked at refute Dr. Saed's research?</p> <p>21 MS. CURRY:</p> <p>22 Object to the form.</p> <p>23 A The only comment I would make on that</p> <p>24 is that this -- and again, I looked at this for</p>
<p style="text-align: right;">Page 419</p> <p>1 MS. CURRY:</p> <p>2 Object to the form.</p> <p>3 A Yeah. I'd have to see that.</p> <p>4 MS. THOMPSON:</p> <p>5 Q Okay.</p> <p>6 A But I'm more familiar with Buz'Zard.</p> <p>7 Q Okay. Well, we just looked at that</p> <p>8 one; right?</p> <p>9 But at least --</p> <p>10 A Yeah.</p> <p>11 Q -- that's what the authors state in</p> <p>12 their introduction --</p> <p>13 A Yeah.</p> <p>14 Q -- regarding talc; correct?</p> <p>15 A Yes.</p> <p>16 Q And, then, we'll just go to the</p> <p>17 conclusion.</p> <p>18 A Uh-huh.</p> <p>19 Q The last paragraph. "In conclusion,</p> <p>20 both IN" -- which is Indian nano particles or</p> <p>21 nano talc -- "and CN" -- which is commercial nano</p> <p>22 talc particles, "significantly induce</p> <p>23 cytotoxicity, oxidative stress and apoptosis in</p> <p>24 human lung epithelial cells."</p>	<p style="text-align: right;">Page 421</p> <p>1 literally five minutes, but I went through some</p> <p>2 of the figures. This paper shows a lot of</p> <p>3 cytotoxicity and apoptosis with the effect of</p> <p>4 talc. That's -- and this is actually in a cancer</p> <p>5 cell line; right? It's human lung epithelial</p> <p>6 cells. I don't think they're -- they're at least</p> <p>7 immortalized. So that strikes me as different</p> <p>8 than the proliferative effect he's describing.</p> <p>9 MS. THOMPSON:</p> <p>10 Q That wasn't my question.</p> <p>11 A Okay.</p> <p>12 Q My question: Do these results refute</p> <p>13 Dr. Saed's work?</p> <p>14 MS. CURRY:</p> <p>15 Object to the form.</p> <p>16 A Well, this is in lung cancer, so it's</p> <p>17 pretty much irrelevant.</p> <p>18 MS. THOMPSON:</p> <p>19 Q And where -- where are you finding that</p> <p>20 it's in lung cancer cells?</p> <p>21 A Human lung epithelial A549 cells. I</p> <p>22 worked with them quite a bit. It's a lung cancer</p> <p>23 cell line. It's an adenocarcinoma. Top of page</p> <p>24 396.</p>

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<p style="text-align: right;">Page 422</p> <p>1 Q Human lung epithelial cells?</p> <p>2 A Uh-huh.</p> <p>3 Q Those are cancer cells?</p> <p>4 A A549, if it's the same A549 which I</p> <p>5 know about, which I think it is, that's an</p> <p>6 adenocarcinoma.</p> <p>7 Q Do you see anywhere in the paper where</p> <p>8 it describes those as cancer cells?</p> <p>9 A Just let me look at the back. I don't</p> <p>10 see it, although I've rushed through this. But I</p> <p>11 don't see it.</p> <p>12 Q I know. I don't see it either.</p> <p>13 They're just described as human lung epithelial</p> <p>14 cells, which doesn't sound like they were</p> <p>15 considered to be cancer cells.</p> <p>16 I'm not sure I got the answer to the</p> <p>17 question "Is there anything in either of these</p> <p>18 Akhtar papers that refutes Dr. Saed's findings?"</p> <p>19 A No.</p> <p>20 MS. CURRY:</p> <p>21 Object to the form.</p> <p>22 MS. THOMPSON:</p> <p>23 Q Do both of these Akhtar papers</p> <p>24 demonstrate biological effect from talc particles</p>	<p style="text-align: right;">Page 424</p> <p>1 MS. CURRY:</p> <p>2 Oh. I'm so sorry. Thank you.</p> <p>3 EXAMINATION</p> <p>4 BY MS. CURRY:</p> <p>5 Q Dr. Birrer, you have reviewed</p> <p>6 Dr. Clarke-Pearson's expert report; correct?</p> <p>7 A Yes.</p> <p>8 Q Do you think his opinions overall are</p> <p>9 based on sound science?</p> <p>10 A No.</p> <p>11 Q Do you defer to him on any issue</p> <p>12 presented in this case?</p> <p>13 A No.</p> <p>14 Q Do you defer to any of the plaintiffs'</p> <p>15 experts on any issues presented in this case?</p> <p>16 A No.</p> <p>17 MS. CURRY:</p> <p>18 I have no further questions.</p> <p>19 Thank you.</p> <p>20 MS. THOMPSON:</p> <p>21 I'm done.</p> <p>22 VIDEOGRAPHER:</p> <p>23 Okay. This concludes this deposition.</p> <p>24 The time is 6:04 p.m. We're off the</p>
<p style="text-align: right;">Page 423</p> <p>1 on cell culture --</p> <p>2 MS. CURRY:</p> <p>3 Object to --</p> <p>4 MS. THOMPSON:</p> <p>5 Q -- lines?</p> <p>6 MS. CURRY:</p> <p>7 Object to the form.</p> <p>8 A I would say yes, that there is some</p> <p>9 activity.</p> <p>10 MS. THOMPSON:</p> <p>11 If we can take just a short break, I</p> <p>12 think I'm finished.</p> <p>13 VIDEOGRAPHER:</p> <p>14 Off the record at 5:48 p.m.</p> <p>15 (OFF THE RECORD.)</p> <p>16 VIDEOGRAPHER:</p> <p>17 We're back on the record at 6:03 p.m.</p> <p>18 MS. THOMPSON:</p> <p>19 Dr. Birrer, I have no further</p> <p>20 questions. Thank you for your time today.</p> <p>21 MS. CURRY:</p> <p>22 I have just a few follow-up questions.</p> <p>23 VIDEOGRAPHER:</p> <p>24 Counsel, your microphone.</p>	<p style="text-align: right;">Page 425</p> <p>1 record.</p> <p>2 (Deposition concluded at 6:04 p.m.)</p> <p>3</p> <p>4</p> <p>5</p> <p>6</p> <p>7</p> <p>8</p> <p>9</p> <p>10</p> <p>11</p> <p>12</p> <p>13</p> <p>14</p> <p>15</p> <p>16</p> <p>17</p> <p>18</p> <p>19</p> <p>20</p> <p>21</p> <p>22</p> <p>23</p> <p>24</p>

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<p>1 CERTIFICATE</p> <p>2 STATE OF ALABAMA)</p> <p>3 COUNTY OF MOBILE)</p> <p>4</p> <p>5 I do hereby certify that the above and</p> <p>6 foregoing transcript of proceedings in the matter</p> <p>7 aforementioned was taken down by me in machine</p> <p>8 shorthand, and the questions and answers thereto</p> <p>9 were reduced to writing under my personal</p> <p>10 supervision, and that the foregoing represents a</p> <p>11 true and correct transcript of the proceedings</p> <p>12 given by said witness upon said hearing.</p> <p>13 I further certify that I am neither of</p> <p>14 counsel nor of kin to the parties to the action,</p> <p>15 nor am I in anywise interested in the result of</p> <p>16 said cause.</p> <p>17 Signed this 22nd day of March, 2019.</p> <p>18</p> <p>19</p> <p>20 LOIS ANNE ROBINSON, RDR</p> <p>21 COURT REPORTER, NOTARY PUBLIC</p> <p>22 STATE OF ALABAMA AT LARGE</p> <p>23 ACCR# 352; EXPIRES 9/30/19</p> <p>24</p>	<p>1 - - - - -</p> <p>2 E R R A T A</p> <p>3 - - - - -</p> <p>4</p> <p>5 PAGE LINE CHANGE</p> <p>6 REASON: _____</p> <p>7</p> <p>8 REASON: _____</p> <p>9</p> <p>10 REASON: _____</p> <p>11</p> <p>12 REASON: _____</p> <p>13</p> <p>14 REASON: _____</p> <p>15</p> <p>16 REASON: _____</p> <p>17</p> <p>18 REASON: _____</p> <p>19</p> <p>20 REASON: _____</p> <p>21</p> <p>22 REASON: _____</p> <p>23</p> <p>24 REASON: _____</p>
<p>Page 427</p> <p>1 INSTRUCTIONS TO WITNESS</p> <p>2</p> <p>3 Please read your deposition</p> <p>4 over carefully and make any necessary</p> <p>5 corrections. You should state the reason</p> <p>6 in the appropriate space on the errata</p> <p>7 sheet for any corrections that are made.</p> <p>8 After doing so, please sign</p> <p>9 the errata sheet and date it.</p> <p>10 You are signing same subject</p> <p>11 to the changes you have noted on the</p> <p>12 errata sheet, which will be attached to</p> <p>13 your deposition.</p> <p>14 It is imperative that you</p> <p>15 return the original errata sheet to the</p> <p>16 deposing attorney within thirty (30) days</p> <p>17 of receipt of the deposition transcript</p> <p>18 by you. If you fail to do so, the</p> <p>19 deposition transcript may be deemed to be</p> <p>20 accurate and may be used in court.</p> <p>21</p> <p>22</p> <p>23</p> <p>24</p>	<p>Page 429</p> <p>1</p> <p>2 ACKNOWLEDGMENT OF DEPONENT</p> <p>3</p> <p>4 I, _____, do</p> <p>5 hereby certify that I have read the</p> <p>6 foregoing pages, and that the same is</p> <p>7 a correct transcription of the answers</p> <p>8 given by me to the questions therein</p> <p>9 propounded, except for the corrections or</p> <p>10 changes in form or substance, if any,</p> <p>11 noted in the attached Errata Sheet.</p> <p>12</p> <p>13</p> <p>14</p> <p>15 _____</p> <p>16 MICHAEL BIRRER, M.D., PH.D. DATE</p> <p>17</p> <p>18 Subscribed and sworn</p> <p>19 to before me this</p> <p>20 _____ day of _____, 20____.</p> <p>21 My commission expires: _____</p> <p>22</p> <p>23 _____</p> <p>24 Notary Public</p>

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Exhibit E

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY**

**IN RE: JOHNSON & JOHNSON TALCUM
POWDER PRODUCTS MARKETING, SALES
PRACTICES AND PRODUCTS LIABILITY
LITIGATION**

MDL NO. 16-2738 (FLW) (LHG)

THIS DOCUMENT RELATES TO ALL CASES

**EXPERT REPORT OF BENJAMIN G. NEEL, MD, PHD
FOR GENERAL CAUSATION *DAUBERT* HEARING**

Date: February 25, 2019



Benjamin G. Neel, M.D., Ph.D.

I. BACKGROUND AND QUALIFICATIONS

I am the Laura and Isaac Perlmutter Director and Professor of Medicine (with tenure) at NYU School of Medicine. In that capacity, I am responsible for all cancer care and research across NYU Langone Health.

In my role at NYU, I oversee my own 13-person research laboratory, which has been continuously funded by NCI/NIH since 1988. My major expertise is in the area of cancer cell signaling, most notably involving protein-tyrosine phosphatases (PTPs). I am generally recognized as a co-founder of the PTP field, and have authored or co-authored multiple major reviews and co-edited a book in this area.

I received my Ph.D. in Viral Oncology at The Rockefeller University in 1982 in the laboratory of Lasker Awardee Hidesaburo Hanafusa, Ph.D., working directly under William S. Hayward, Ph.D. My thesis work established that slowly transforming RNA tumor viruses caused cancer by inserting themselves next to, and activating, the cellular proto-oncogene *c-Myc*. This finding served as the paradigm for oncogenesis by all such viruses and anticipated the subsequent discovery that many chromosomal translocations (rearrangements) cause cancer in humans by a similar “promoter/enhancer” mechanism. Dr. Hayward was the co-recipient of the Bristol-Myers Squibb award for this discovery.

I received my M.D. from Cornell University Medical School (now Weill-Cornell) in 1983, and completed medical internship and residency training at the former Beth Israel Hospital (now Beth Israel Deaconess Medical Center (BIDMC)) from 1983-85. I am a Diplomate of the American Board of Internal Medicine (board-certification). From 1985-1988, I pursued post-doctoral studies as a Leukemia Society Special Fellow with Lasker Awardee Raymond L. Erikson, Ph.D., in the Department of Cell and Developmental Biology at Harvard University.

In 1988, I was appointed Assistant Professor of Medicine at Harvard Medical School (HMS), and started my own research laboratory at Beth Israel Hospital. I rose through the ranks at HMS, becoming Professor of Medicine in 1999, and also serving as Director of the Cancer Biology Program, from 1994, and Deputy Director for Basic Research, Hematology-Oncology at BIDMC, beginning in 2003. In 2006, I was appointed to the William B. Castle Chair of Medicine at HMS. Under my leadership, Hematology-Oncology rose from the least-funded to the top-funded (in NIH/NCI grants) division in the Department of Medicine at BIDMC. I also recruited three new junior faculty, two of whom are now Professors of Medicine at HMS.

In 2007, I became Director of Research at Princess Margaret Cancer Center (PMCC) in Toronto, Canada, and Senior Scientist and Canada Research Chair, Tier 1, in the Departments of Medical Biophysics and Biochemistry at the University of Toronto. In that capacity, I recruited more than 20 new investigators, and established new programs in Clinical Cancer Genomics, Epigenetics, Computational Biology and Tumor Immunology/Immune Therapy. During my tenure, PMCC ranked 3rd or 4th year over year in percentage of high-impact publications among North American cancer centers, and grant and philanthropic funding each increased by more than 50% on a yearly basis.

During my time at PMCC, my group also developed a significant interest in ovarian cancer pathogenesis and functional genomics. I have authored several papers in this area, chaired the Current Topics in Ovarian Cancer session at the American Association for Cancer Research (AACR) annual meeting in 2014 and co-chaired the AACR Ovarian Cancer Conference in 2015. Overall, I have published 234 peer-reviewed primary manuscripts and 33 invited reviews, which together have attracted more than 45,000 citations. I have an h-index of 107 and an i10 of 236.

Since assuming my position at NYU Langone in January 2015, I have recruited 38 new investigators from external institutions, restructured our entire leadership team and successfully renewed our NCI Cancer Center Support Grant with a score of “Outstanding” and “Comprehensive Cancer Center” designation.

In addition to my institutional experiences, I have had a number of national and international leadership roles. I have chaired or co-chaired numerous important scientific meetings, including Gordon Conferences, FASEB meetings, and Cold Spring Harbor (CSH) meetings, all of which are major meetings in the fields of cancer biology and signal transduction. I am currently co-chair of the CSH Meeting on Cancer, through 2021. Chairing/co-chairing such conferences is generally recognized as indicative of world leadership in the field. In 2012, I was the Program Chair for the AACR annual meeting, which attracts nearly 20,000 cancer researchers from around the world. As Program Chair, I was responsible for selecting leaders for all of the sessions, and ultimately responsible for the entire meeting program and its execution. From 2012-2015, I served as an elected member of the AACR Board of Directors. I have been a member on several AACR award selection committees, and just completed service as Chair of the committee to select the AACR Lifetime Achievement Award. I also have served as a full member on two NIH study sections, and as an external reviewer of the intramural program at NCI-Frederick, program project grants, and Cancer Center grants. I am a member of the external advisory boards of 3 NCI-designated Comprehensive Cancer Centers (Columbia, Northwestern, Rutgers-CINJ). I also was an Editor of the journal *Molecular and Cellular Biology* from 1991 to 2000, and currently serve on the editorial boards of multiple major cancer and cellular/molecular biology journals, including the two most highly rated specialized journals for Cancer Biology, *Cancer Cell* and *Cancer Discovery*.

I have also been fortunate to receive several awards in recognition of my research. I was the first recipient of the Gertrude Elion Award from the AACR. I have been elected to the American Association of Physicians, received the Premier of Ontario’s Summit Award (the highest scientific award in Ontario), and held an NIH MERIT award from 2003-2013.

Overall, my own research and multiple leadership experiences have given me broad expertise in cancer biology and medicine, as well as detailed, specific expertise in signal transduction and ovarian cancer pathobiology.

A complete curriculum vitae is attached as an appendix to this report.

I am being compensated at a rate of \$750 per hour for my expert work in this litigation. All of the opinions in this report are stated to a reasonable degree of scientific certainty.

II. WHAT IS CANCER?

A brief overview of normal cellular regulation: Our cells are complex machines, and thus are subject to multiple – and intricate – levels of regulation. The cellular “control center” is the nucleus, which houses 46 chromosomes (23 pairs), composed of “chromatin.” Chromatin comprises DNA wrapped around specific proteins, called histones. “Genes” are units of DNA of variable length that encode the instructions for making proteins, the ultimate workhorses of cells. These instructions are transmitted from the nucleus by messenger RNA (mRNA) to protein synthesis machines, called ribosomes, in the cytosol. The genetic content of an organism is termed its “genome,” and to maintain genomic integrity, when a cell divides, it must replicate its DNA perfectly and reassemble it properly into chromosomes.

Although all cells contain the same genes, different types of cells express different mRNAs, and consequently, distinct proteins. For example, blood cells, skin cells and heart cells express different mRNAs and proteins. Such “differential gene expression” is achieved in multiple ways. Much of the genome comprises DNA (“regulatory regions”) that binds proteins called “transcription factors,” which instruct genes to turn on or turn off. Transcription factors bind specific sequences in the DNA, known as “enhancers” and “promoters,” respectively. Another, more recently described level of gene regulation, often termed “epigenetic,” is mediated at the level of histones or DNA. Histones undergo chemical modifications, such as acetylation, methylation, and phosphorylation, and/or have other proteins (ubiquitin, SUMO) attached to, or removed from, them. This “histone code” regulates the accessibility of different parts of the DNA to transcription factors. Large regions of the genome can be “looped” together to render them susceptible to the same histone modifications, and thereby control blocks of genes together. Looping is mediated by the binding of two proteins, called CTCF and cohesin, which also bind to specific regions (CTCF/cohesin binding sites). Looping and histone movements require “chromatin remodeling,” carried out by so-called “SWI/SNF chromatin remodeling complexes.” Long non-coding RNAs (lncRNAs) also may play important roles in controlling opening and closing of specific regions of chromatin.

These multiple levels of control leave some regions of the genome “open,” and others closed or “compacted.” For a gene to be expressed, it must lie in open chromatin, and its key transcription factors must be expressed and bound to its enhancer/promoter regions. Genes that lie in closed or compacted chromatin can only be expressed if the chromatin is opened by altered epigenetic regulation. DNA, which consists of adenines, guanines, thymine and cytosine residues, can be methylated on specific cytosines. DNA methylation also helps control its packaging into open or closed chromatin, and thereby its access to transcription factors. In general, high levels of methylation (hypermethylation) are associated with closed, inactive chromatin, whereas hypomethylation correlates with open, active gene regions.

Gene expression is also regulated by RNA splicing and microRNAs (miRNAs). Nearly all protein-coding genes are divided into “exons” and “introns.” When a gene is expressed, all of its exons and introns are made into an initial “pre-mRNA,” which is then “spliced” by a multi-protein complex called the “spliceosome.” Splicing stitches exons together, while removing introns. Although most exons (“coding exons”) contain the coding information for proteins, others are “non-coding.” Some non-coding exons bind miRNAs, which inhibit translation of that mRNA by the ribosome, and ultimately cause the mRNA to be degraded. Some genes undergo

“alternative splicing,” whereby specific exons are shuffled in or out in different physiological states or cell contexts. These “alternative splice products” can result in the expression of different proteins from the same gene. Thus, while there are only about 20,000 human genes, these likely encode around 60-80,000 human proteins. Alternative splicing also can leave a miRNA-binding exon in or out of an mRNA, thereby affecting the level of its cognate protein.

Once synthesized, proteins perform all major functions in cells. These include the generation and utilization of energy (“metabolism”), specialized cell functions such as cell movement, antibody production, defense against parasites and other microorganisms, digestion, pumping of blood and food, and reproduction, among others. Specific proteins also enable cells to respond correctly to signals in the external environment. For example, cells receive specific signals known as “growth factors and cytokines,” to begin the process of cell growth and division. They also receive other “growth inhibitory” signals. These analog signals are integrated, via a process termed “signal transduction,” into digital cellular decisions: should the cell divide, move, contract, etc.? Most of these signals are transmitted from specific proteins on the cell membrane termed “receptors” through downstream signaling molecules, to the cell nucleus. Ultimately, signal transduction results in modifications of transcription factors or epigenetic regulators, and changes in gene expression.

Hence, while cellular information flow follows the “Central Dogma” of molecular biology, DNA->RNA->protein, there are many devils in the dogma’s details. For a given protein to be expressed, its gene must reside within open chromatin, and transcription factors that activate its cognate gene must be present and active. The level of that protein is determined by how strongly the particular transcription factor engages the mRNA synthesis machinery, and whether or not miRNAs that control its mRNA are present. There also are additional levels of control of protein synthesis and degradation (“translational” and “post-translational” control, respectively). Proteins, in turn, perform all of the key functions of the cell, including the transmission of signals back to the cellular control center in the nucleus. Remarkably, these processes usually function seamlessly and continuously throughout human life. When they malfunction, however, disease, including cancer, ensues.

Cancer is a disease of the genome: Many diseases result from external pathogens (e.g., bacteria, viruses, parasites) that disrupt normal body functions. Cancer, however, is a disease of the genome, caused by “mutations” that affect the intricate control mechanisms described above. Mutations are structural changes in DNA that occur in multiple varieties. “Point mutations” affect single DNA residues, and depending upon their precise location, can have distinct effects. If they affect coding regions of genes, point mutations can increase (“gain-of-function”) or decrease (“loss-of-function”) a protein’s normal activity. Alternatively, point mutations can affect key regulatory regions. For example, mutations that alter CTCF binding sites have been reported; these can lead to altered chromatin structure and aberrant gene expression, as can mutations that affect chromatin remodeling complexes and mutations in CTCF itself. “Structural variants” also contribute to cancer. Chromosomes can break and rejoin incorrectly, resulting in part of one chromosome becoming attached to another, an aberration known as a “translocation.” Some translocations place a gene under the regulatory control of another gene, resulting in inappropriate expression. Others result in “fusion proteins,” in which a piece of one protein is grafted onto another. Fusion proteins typically drive a highly regulated protein into a

constitutively “on” state. Other times, chromosomes –or regions within chromosomes – undergo “amplification” or “deletion.” Amplifications result in an increase in the “copy number” of a specific gene or genes – and thus are gain-of-function mutations. Deletions result in decrease or absence of a specific gene product. Collectively, deletions and amplifications are termed “copy number abnormalities” (CNAs).

Cancer-causing mutations (point mutations, translocations, CNAs) affect specific genes, known as “oncogenes” and “tumor-suppressor” genes. Oncogenes undergo gain-of-function mutations, and encode proteins that tell cells to grow, divide, send out signals to promote new blood formation (“angiogenesis”), and/or escape the immune system. Some oncogenes inhibit a process called “programmed cell death,” which directs cells to commit suicide if they have suffered too much damage. Representative oncogenes include the BCR/ABL fusion protein, the product of the so-called “Philadelphia chromosome” in chronic myelogenous leukemia, which encodes a constitutively active “kinase” and is the target of the drugs Imatinib and Dasatinib, and HER2, which is amplified in ~20% of breast cancer cases (and at a lower rate in some other cancers) and is the target of the drug Herceptin. Tumor suppressor genes undergo loss-of-function mutations, and come in two general categories. Some, such as the so-called “retinoblastoma gene product” (RB), and the *PTEN* gene product, encode proteins that tell cells to stop growing. Others direct DNA repair; these are sometimes termed “caretaker genes.” For example, *BRCA1* and *BRCA2* are tumor suppressor genes whose products control a specific type of DNA repair called “homologous recombination.” Other tumor suppressor genes control “mismatch repair.” The *TP53* tumor suppressor gene is one of the most frequently altered genes in human cancer, and is mutated in virtually all high grade serous ovarian carcinomas. The *TP53* gene product (TP53) tells cells to stop growing, activates the DNA repair machinery, and directs cell death if the DNA damage is not repaired. Because of its multiple, critical functions in maintaining genome integrity, TP53 has been termed the “guardian of the genome” [1-4].

Large-scale sequencing efforts have identified nearly 600 genes whose mutation clearly contributes to human cancer, and many others that might contribute (<https://cancer.sanger.ac.uk/cosmic>). Established cancer-causing mutations affect all of the major cellular regulatory processes described above, including alterations of histone modifications, DNA methylation, chromatin remodeling proteins, CTCF binding, transcription factor binding and/or expression, miRNA and lncRNA expression splicing, and the expression and/or activity of signal transduction proteins [4].

Fortunately, like any complex machine, cells engage multiple “back-up” systems whenever they incur a mutation in an oncogene or tumor suppressor gene. Consequently, 6-8 independent genetic changes must occur before a cell’s multiple failsafe mechanisms are breached and malignancy develops [5]. Typically, these include mutations in some combination of oncogenes and tumor suppressor genes. They also can include combinations of point mutations and structural variants, although most tumors are driven mainly by one or the other of these mutational processes. In some (but not all) types of cancer, “pre-malignant” lesions can be visualized under the microscope (histologically); DNA sequencing shows that such lesions have subsets of the mutations seen in full-blown cancers.

Cancer is a genetic disease, but most cancer is not inherited: All cancers are “genetic” (i.e., caused by mutations in (multiple) genes), but only a minority are “inherited” (i.e., caused by mutations that occur in a patient’s parents and are transmitted through the “germ cells” (sperm or eggs)) [6, 7]. Two general types of inherited variants contribute to increased cancer risk. Strong cancer risk often shows “autosomal dominant” inheritance, which means that inheriting one copy of the defective gene increases risk. Classic examples include: mutations of *BRCA1* or *BRCA2*, which increase susceptibility to breast and ovarian cancer, but also several other malignancies (pancreas, prostate, melanoma, etc.), *TP53* mutations, which cause “Li-Fraumeni syndrome,” and mutations in one of several genes involved in mismatch repair, which cause “Lynch syndrome.” Each of these can increase the risk of developing different types of ovarian cancer. Although germ line mutations typically show autosomal dominant inheritance, both copies of the gene usually must be inactivated for cancer to occur. Loss of the second copy (“allele”) can occur in multiple ways, including loss of all or part of the chromosome containing the normal copy, mutation, a process known as “gene conversion,” or epigenetic silencing of the chromatin containing the normal gene. Although *BRCA1* and *BRCA2* mutations show autosomal dominant inheritance, only some patients inheriting such mutations develop breast or ovarian cancer; hence, even these strong risk genes show “incomplete penetrance.”

Beyond strong cancer susceptibility genes, multiple single nucleotide polymorphisms (SNPs) each confer slightly increased risk of specific (or multiple) cancers [8]. SNPs, as their name implies, are variations in DNA sequence that occur between individuals. Most of these are normal variants that reflect the wide diversity of the human population; on average, any two unrelated individuals have a sequence difference approximately every 300 nucleotides (the total size of the human genome is 6 billion nucleotide pairs). Most SNPs are in non-coding regions, but protein-coding SNPs occur about every 900-1000 nucleotides. Although they are quite frequent, the overwhelming majority of SNPs have no pathological significance. Others, though, especially in combination, contribute to familial predisposition to cancer. Most risk-conferring SNPs have been identified by genome-wide association studies (GWAS), which simultaneously correlate large batteries of SNPs against different disease states. The most recent GWAS compendium lists ~100 SNPs that affect the risk of high grade serous ovarian cancer (<https://www.ebi.ac.uk/gwas/>). Notably, to be sure that SNPs are associated with a trait, one must correct statistics for multiple comparisons; i.e., the chance that if one measures enough parameters, some will seem to be associated by chance. Consequently, only SNPs that attain “genome-wide significance” are assured of association with cancer; genome-wide significance means a “P-value” of $<10^{-8}$.

Only 5-10% of cancers have a strong inherited predisposition (i.e., are due to inheritance of autosomal dominant risk alleles). Nevertheless, comparison of cancer incidence in identical and fraternal twins suggests that up to a third of all cancers have some familial component, with some cancers having even higher familial contributions. A recent large study of Nordic twins suggests that as much as 39% of ovarian cancer might have a familial component, although the error in this estimate is large (23-55%), and the study did not differentiate between different types of ovarian cancer [8].

Most cancer-causing mutations are “somatic,” meaning mutations occurring in non-germ (somatic) cells after birth. These result from DNA damage or errors in replication that exceed the

cellular repair capacity, occur sporadically, and accumulate over time. For this reason, the greatest contributor to cancer risk is age. Strong environmental “carcinogens,” such as cigarette smoke, X-rays and ultraviolet light, increase the rate of DNA damage, making it more likely that the damage will go unrepaired and result in a cancer-causing mutation. Agents that directly detect DNA damage can be detected by surrogate “genotoxicity” assays [9], such as the “Ames test.” Notably, however, even genotoxic compounds typically demonstrate a dose-response in their ability to cause cancer, for the simple reason that powerful cellular repair pathways are always attempting to reverse the damage that these agents cause. Because cells have this remarkable capacity to repair DNA, DNA damage is cumulative, and multiple genes must be mutated to generate a malignancy, the more exposure that one has to a genotoxic substance, the more likely one is to develop cancer. For example, the risk of lung cancer in cigarette smokers is related to “pack-years” (the number of packs smoked per day X number of years of smoking), and substantially increased risk is seen above 20 pack-years [10].

More recently, “mutational signatures” of several carcinogens have been discerned by DNA sequence analysis of tumors, which can reveal specific patterns of damage caused by these agents [11]. Agents or conditions that lead to increased inflammation can result in the production of “reactive oxygen species” (ROS), which can damage DNA and lead to mutations under certain conditions. Conditions like obesity, which is now the major risk factor for cancer in the United States, probably contribute to cancer at least in part by promoting inflammation and excess ROS generation. Nevertheless, the majority of cellular ROS are generated as part of normal physiological processes, particularly mitochondrial respiration [12]. Consequently, there is no reason to infer that a person who develops cancer has been exposed to a cancer-causing chemical or physical agent in the environment. Rather, most cancer-causing somatic mutations probably occur as a consequence of unrepaired errors in DNA replication, and are thus mere bad luck. Put another way, the cancer-causing environment is our own body – and the enemy lies within [13-16].

Cancer disrupts normal cellular regulation: When a cell has suffered a sufficient number of cancer-causing mutations, its normal function is disrupted in multiple ways, which differ for different types of cancer. In general, however, malignant cells share several “hallmarks” of cancer [5].

- Normal cells typically need external growth signals to proliferate. Cancer cells generate their own growth signals or become autonomous of external growth signals in other ways.
- Normal cells respond to external growth-inhibitory signals. Cancer cells ignore such signals.
- Normal cells self-destruct when they suffer DNA damage that is unrepairable. Cancer cells disable the self-destruct mechanism.
- Most normal cells divide only a limited number of times. Cancer cells can have markedly extended or even unlimited proliferative capacity.

- Normal cells replicate their genomes with high fidelity. Genomic integrity is compromised in cancer cells, and this lack of genome stability can result in ongoing genetic change and escape from therapy.
- Normal cells do not usually send signals to surrounding blood vessel cells to make new blood vessels. Tumors typically send multiple such signals, via a process known as tumor angiogenesis (the formation of new blood vessels). Angiogenesis enables tumors to create their own blood supply as they expand beyond their normal size and location.
- Normal cells typically are located within a defined area. For example, “epithelial cells” (the cells that line body tubes and cavities) usually rest on top of a “basement” membrane that separates them from underlying connective tissue and blood vessels. Cancer cells can invade through this basement membrane, and also can spread to, and establish residence in, other organs, a process known as “metastasis.”
- When normal cells express abnormal proteins – e.g., when they are infected with a virus or other pathogen – they display these proteins to the immune system, which can eliminate the cells. Cancer cells develop multiple strategies to evade the immune system.
- Normal cells typically have defining characteristics that make them look unique. For example, different cell types within the lung or gut have a distinct appearance under the microscope, because they have different functions. Cancer cells, to different extents, lose such “differentiated” features.
- Cancer cells often use fuels differently than normal cells, enabling them to survive in abnormal, and often hostile, milieus.

Cancer is not a single disease – or even a single type of disease: “Cancer” is not one disease, but probably hundreds. Pathologists sub-divide cancer in multiple ways. The simplest criterion is based on the type of cell from which the malignancy originates. Epithelia are the cells that line our body tubes and glands. Skin and the lining of our mouth, throat, lung, gastrointestinal tract, urinary tract, and reproductive organs, are composed of epithelial cells. “Carcinomas” are tumors that originate in epithelial tissues, and are then specified further by the (presumed) cell-of-origin (“breast” cancer, “lung” cancer, “bladder” cancer, etc.). “Sarcomas” initiate in connective tissue (mesenchymal) cells, such as bone (osteosarcoma), cartilage (chondrosarcoma), or striated or smooth muscle (rhabdomyosarcoma, leiomyosarcoma). Leukemias and lymphomas involve blood-forming cells. Pathologists also refer to “tumor grade,” which, as mentioned above, reflects the extent to which the tumor cell has lost the “differentiated features” of the cell-of-origin. High grade tumors resemble the normal tissue less than low grade tumors. A tumor’s “stage” typically reflects its size and the extent to which it has spread beyond its initial tissue boundary. Each tumor type has its own staging system, which usually goes from Stage I to IV. Staging, in turn, is based on the “Tumor, Nodes, Metastasis” criteria. For example, a Stage I ovarian cancer is confined to the ovary or fallopian tube, and has not spread to the lymph nodes, whereas a Stage IV tumor has spread beyond the pelvic cavity to other organs.

Although microscopic examination, grading and staging remain essential components of cancer diagnosis and therapy recommendations, with the advent of the molecular era, we realize that (microscopic) appearance isn't everything – in fact, it is relatively little. Instead, tumors from different organs can have similar molecular defects, whereas those from the same organ can be quite different. For example, high grade serous ovarian cancer is genetically – and functionally – more similar to triple negative breast cancer than to other types of ovarian cancer [17, 18]. These differences in the genetic architecture of different tumors also imply distinct underlying mutational processes. Stated simply, it is highly unlikely that tumors that have different genomic defects/mutational signatures are caused by the same mutational agent(s).

Ovarian cancer is not a single disease – and in most cases, it is not even “ovarian”: Even at the microscopic level, it is clear that ovarian cancer is more than one disease [19]. “Ovarian” tumors were initially thought to originate from one of the three cell types found within gonadal tissue: sex cord-stromal cells, germ cells and ovarian surface-epithelial cells. As described below, most “ovarian” tumors are now believed to originate from other tissues that implant on the ovarian surface early in their development as neoplasms. Nevertheless, the old histology-based nomenclature persists.

The vast majority (90%) of tumors of the ovary are “Epithelial ovarian carcinomas” (EOC) [19]. These, in turn can be sub-divided into high grade serous (~70%), mucinous (~3%), endometrioid (~10%), clear cell (10%) and low grade serous (<5%) carcinomas. The most common EOC, high grade serous ovarian carcinoma (HGSOC), is, unfortunately, also the most lethal gynecologic malignancy and the 5th-most-common cause of cancer death in women in the United States. The EOC subtypes differ in likely cell-of-origin, genomic abnormalities, metastatic potential, treatment response and therefore, prognosis. This disparity in their characteristics, and particularly, their distinct mutational profiles (see below), makes it almost certain that they differ in pathogenesis.

The remaining 10% of ovarian cancers comprise the germ cell and sex cord-stromal tumors, respectively. Germ cell tumors (~1-2% of all ovarian cancers) originate from defective germ cells or their derivatives (trophoblast, embryonal carcinomas). Sex cord-stromal tumors (~8-9% of ovarian cancer) arise from the tissues that surround and support the germ cells (granulosa cells, theca cells, fibocytes). Plaintiffs do not allege that talc causes this class of tumors, so I will not discuss them further.

Epithelial ovarian cancers fall into two general classes: Recent re-evaluation of EOC pathobiology suggest that these tumors should be re-classified into two large groups [20-22]. “Type I” tumors, which include low grade serous ovarian cancer (LGSOC), mucinous carcinoma (MC), endometrioid carcinoma (EC), and clear cell carcinoma (CCC), develop more slowly and through defined intermediate stages of differing malignant potential, are generally more genetically stable and less aggressive, and are usually detected at an early stage (Stage I). Increasing evidence also suggests that these tumors arise from different locations and cell types [22-26]. EC and CCC are thought to derive from endometriotic lesions from the uterus that implant on the ovarian surface and undergo further malignant transformation. LGSOC probably arises from fingertip-like projections (“fimbria”) at the ends of the fallopian tube (FT), although an ovarian surface epithelium (OSE) origin has not been excluded, and MC might arise from the

junction of the fallopian tube and the peritoneum (tubal-mesothelial junction) or from ectopic sites like the GI tract. Type II tumors comprise HGSOC, undifferentiated carcinomas and rare carcinosarcomas (the latter two are probably variants of HGSOC). At least 60% of these originate in the FT fimbria, and it is possible that they all do. HGSOC are highly aggressive, genetically unstable, and unlike Type I tumors, often appear without an obvious precursor lesion. However, close inspection of the fimbria can often (at least 60% of the time) reveal such a precursor, which is termed serous tubal intraepithelial carcinoma (STICs); indeed, it was the discovery of STIC lesions in *BRCA1/2*-mutant patients undergoing prophylactic removal of their fallopian tubes and ovaries that led to the FT “cell-of origin” concept [27-32].

Subsequent, detailed DNA sequencing studies of STICs and full-blown ovarian cancers have shown that in most cases, STICs contain only some of the genetic abnormalities seen in the bulk tumor [33, 34]. Scientists interpret such results as indicating that the STIC gave rise to the bulk tumor, arguing in favor of an FT origin for HGSOC. However, in other cases, tumors in the FT show more genomic changes than the ovarian mass, which suggests that the tumor-initiating event took place in (on) the ovary or elsewhere and then metastasized to the FT [35]. Furthermore, in the remaining 40% of HGSOC, no precursor lesion can be identified, leaving open the possibility that the tumor originated within the tumor mass(es) seen in the ovary. Comparison of gene expression in human normal ovarian surface epithelial cells, normal human fallopian tube epithelium (“FTE”), and a large panel of HGSOC indicates that a significant fraction (15-30%) of HGSOC appears more similar to OSE than to FTE [26]. Also, a recent study from our laboratory, which is under review (<http://biorxiv.org/cgi/content/short/481200v1>), shows unambiguously that either OSE or FTE can be transformed to generate HGSOC in mice. Thus, it is conceivable that not only do individual HGSOC cases have different combinations of mutations, but some might originate from the FTE, whereas others originate from OSE.

Finally, HGSOC, because it is often quite undifferentiated, or shows mesenchymal differentiation, can be difficult to discern from peritoneal mesothelioma under the microscope. Special immunohistochemical stains (e.g., for the marker PAX8) have made this differential diagnosis far more facile in modern pathology laboratories [36]. Nevertheless, mesothelioma originates from a distinct cell type (mesothelium), has distinct genomic abnormalities and likely has distinct causes. Whereas asbestos clearly causes pleural (chest wall) and peritoneal mesothelioma, this does not imply that it causes *bona fide* ovarian cancer.

The different types of EOC are caused by distinct mutations and mutational types:
Type I tumors typically feature mutations in components of signal transduction pathways [20, 25]. For example, LGSOC and MC frequently have gain-of-function point mutations in *BRAF* or *KRAS*. *KRAS* and *BRAF* participate in the same signaling pathway downstream of most growth factor receptors, with *KRAS* functioning to activate *BRAF*. *KRAS* acts as a type of molecular “switch,” oscillating between an “on” *KRAS*-GTP state and an “off” *KRAS*-GDP state. When growth factors are present, *KRAS* is switched on, but then decays to the off state. Gain-of-function mutations cause *KRAS* to “lock” into the “on” state, so that the cell thinks that it is always getting a growth factor signal. *KRAS*-GTP binds to, and activates, *BRAF*. The gain-of-function mutations in *BRAF*-mutant Type I ovarian tumors render *BRAF* active in the absence of an upstream growth factor/*KRAS* signal. EC and CC often have loss-of-function mutations in *ARID1A*, which encodes a chromatin remodeling protein, activating mutations in β -catenin, a

transcription factor that mediates signals from WNT growth factors, and/or gain of function mutations in *PIK3CA* or loss-of-function mutations in *PTEN*. *PIK3CA* produces a signaling lipid, phosphatidylinositol-3-phosphate (PI3P), that is also evoked by growth factor signals, whereas *PTEN* encodes a protein (enzyme) that inactivates PI3P. EC can also be associated with Lynch syndrome, whereas the other Type I tumors show no such association. MC can have gain-of-function mutations in *KRAS* or *BRAF* or amplification of *HER2/ERBB2*, a growth factor receptor also amplified in 20% of breast cancer cases. *TP53* mutations are rare in Type I tumors, and they have relatively stable and “quiet” genomes, with few CNAs or rearrangements.

Type II tumors, by contrast, uniformly have *TP53* mutations or deletions [37], and reflecting *TP53*’s “guardian of the genome” role [38, 39], these tumors look as if a bomb has been dropped in their genomes [40]. There are multiple CNAs, including amplifications, deletions, translocations and fusions. HGSOC cells are highly aneuploid (i.e., have the wrong number of chromosomes) and also have multiple epigenetic changes from normal FT cells. As noted above, up to 10% of HGSOC patients have germline *BRCA1* or *BRCA2* mutation, but *BRCA1/2* are somatically mutated or epigenetically silenced in up to 20% of HGSOC. Other frequent mutations include *PTEN* deletions, *PIK3CA* or *KRAS* amplifications (although point mutations in these genes are rare, unlike in Type I tumors), *NOTCH3* (a type of receptor) or *CYCLIN E* (and cell cycle regulator) amplification and *FOXM1* (a key transcription factor) deletions.

The high degree of genomic abnormality and instability in HGSOC reflects the mutations that are found in this disease. *TP53*, as mentioned before, is often termed the guardian of the genome because of its critical role in maintaining genomic integrity [38, 39]. When *TP53* is defective, multiple genomic abnormalities can accumulate without the cell receiving a “self-destruct” signal. *BRCA1/2* play critical, direct roles in a specific type of DNA repair, termed homologous recombination repair (HRR) [41]. When cells are defective in HRR, they resort to back up, mutation-causing pathways [42].

Taken together, these findings clearly show that different types of ovarian cancer originate in different cell types that suffer different types of mutations, which are unlikely to be caused by the same environmental agent. *Studies, including epidemiological reports, that treat “ovarian cancer” as a single entity, should, in my opinion, be viewed with skepticism.*

Multiple factors, rather than a single cause, likely contribute to ovarian cancer generation: It is difficult to attribute a specific case of cancer to a single cause. Even in smokers, lung cancer is not inevitable, as we know from individuals who have smoked for many years and yet have not developed cancer. Rather, for any cancer, it is only meaningful to speak in terms of exposures that increase risk. It is also important to quantify such risks if it is possible to do so in a scientific way. Risk factors can generally be grouped into genetic and environmental factors. Not surprisingly, both types of risk factors differ for different types of tumors. Moreover, given the multiple lines of evidence, discussed above, that ovarian cancer arises in different cell types as a consequence of distinct mutational events, it should be equally unsurprising that different subtypes of the disease are associated with different risk factors.

It is also important to distinguish *association* between a risk factor and a disease, and a demonstrated causal association. The former means that two events occur more frequently than expected by chance, whereas the latter means that one event causes the other. Two events can occur in common and not be causally related, if one event occurs in association with an undefined causal association. For example, one might find an association between a baby drinking juice and the incidence of a certain disease, and jump to the conclusion that the juice is causing the disease. However, it could be that the juice is almost always imbibed from a plastic bottle and, by virtue of its acidic character, causes other disease-evoking agents to leak from the plastic. To truly demonstrate a causal association requires a plausible, demonstrable biological mechanism of disease. In other words, one must avoid attributing guilt by association to fellow travelers.

There are several clearly established risk factors for all ovarian cancer, and others for specific types (reviewed in [43]). As for almost all cancers, age is a major risk factor: the older a woman is, the more likely she is to accumulate the mutations that lead to ovarian cancer. Genetic risk factors for ovarian cancer were described above and will only be reiterated briefly here. Strong risk is conferred by mutations in *BRCA1* (44% lifetime risk, compared with 1.3% overall), *BRCA2* (27% risk), or other genes involved in HRR (e.g., *BRIP1*, *RAD51C*, *RAD51D*; 5-12% lifetime risk each). These mutations predominantly increase the risk of HGSOC. Lynch syndrome mutations are associated with EC and CCC. Risk SNPs also contribute, but even including these, based on the aforementioned twin studies, less than half of the familial risk can be assigned at present. Nevertheless, in predicting any individual's risk of developing ovarian cancer, these genetic contributions must be considered.

Endometriosis is a risk factor, but only for CC and EC, reflective of the currently accepted pathogenic mechanisms for these diseases (reviewed in [43]). Parity (giving birth) is among the best accepted protective factors. Two major hypotheses have been proposed to explain these observations: incessant ovulation and the gonadotrophin hypothesis. With every ovulation event, there is damage to the OSE that must be repaired; the incessant ovulation hypothesis holds that mistakes can be made during this repair process, leading to mutations. Ovulation is also proposed to damage the FTE fimbria, accommodating the more recent evidence that FT is the site of origin for HGSOC and LGSOC. The gonadotrophin hypothesis argues that luteinizing hormone (LH) and/or follicle stimulating hormone (FSH), rather than ovulation *per se*, can stimulate the relevant target cells to undergo transformation. Early menarche, nulliparity and late menopause, all of which lead to longer periods of unopposed menstrual cycling, are often said to be associated with increased risk of ovarian cancer (reviewed in [43]). However, there are conflicting studies on this issue, and overall, the effect is likely to be small. Infertility might also increase risk, although "infertility" has multiple causes, only some of which might be relevant. Also, it can be difficult to distinguish the effects of infertility from the effects of drugs used to treat this condition. Conversely, the use of oral contraceptives reduces risk. Because LH and FSH direct the normal menstrual cycle, it is difficult to distinguish between these models, as increased exposure to LH and FSH occur together with ovulation in women who have early menarche, late menopause or nulliparity. Regardless, it should be noted that neither of these proposed mechanisms requires any external agent to promote cancer development.

Certain gynecologic procedures or therapies also affect the risk of ovarian cancer. Some studies indicate hysterectomy may reduce risk and bilateral tubal ligation reduces risk by approximately 20-30%, although risk reduction is greatest for EC and CCC, consistent with their proposed pathogenesis (reviewed in [43]). Bilateral oophorectomy markedly lowers risk, which might seem tautological at first, but need not be if the cell-of-origin for different types of OC is not the OSE. Rather, these findings suggest that some factor in the ovaries or the ovarian environment itself is necessary for cancer to develop. Conversely, post-menopausal hormone therapy, especially with estrogen alone, increases risk, with the increase in risk possibly greater for EC and CCC. Whether combined estrogen/progestin also increases risk is less clear, and in any event, the magnitude of the increase is likely to be less.

Finally, lifestyle factors can affect the risk of some subtypes of ovarian cancer. Obesity increases the risk for non-HGSOC, and smoking increases the risk of MC, but has no apparent effect on other subtypes. All of these factors are relevant to individual risk, and it is difficult to control them all when comparing two patient populations. This difficulty, in turn, makes it hard to interpret apparent small increases in risk in epidemiologic studies, particularly when the results of such studies are inconsistent.

III. TALC AND OVARIAN CANCER

Opinion: Talc is not genotoxic, does not cause mutations, does not cause inflammation in the female genitourinary tract and has not been shown to cause ovarian cancer.

Talc is chemically inert and non-genotoxic: Talc is a plate-like magnesium silicate that is chemically inert. It does not score as positive (i.e., cause mutations) in standard genotoxicity assays [44]. Talc is present ubiquitously in foods, such as chewing gum, candies, cured meat, olive oil, ceramics, papers, inks, soaps, plastics, cosmetics and other products [44]. The FDA regulates talc and rejected proposals to add ovarian cancer warnings as recently as 2014 (Letter from Food & Drug Admin., Dep't of Health & Human Servs., to Samuel S. Epstein, M.D., Cancer Prevention Coalition, University of Illinois - Chicago School of Public Health (Apr. 1, 2014)). The IARC reviewed the literature on talc in 2010 and classified it as “possibly carcinogenic (class 2B),” which, according to its definition, means that “there is limited evidence of carcinogenicity in humans *and* less than sufficient evidence of carcinogenicity in experimental animals.” (Int'l Agency For Research On Cancer, World Health Org., *93 Monographs on the Evaluation of Carcinogenic Risks to Humans: Carbon Black, Titanium Dioxide, and Talc* at 35 (2010).) Very recently, Health Canada again reviewed the literature surrounding talc and ovarian cancer, stating in a draft screening assessment that talc was “possibly carcinogenic” [45]. I carefully reviewed the Taher et al. manuscript that was funded by Health Canada, which is under review for publication but has been released to the public. It focuses primarily on a meta-analysis of the numerous epidemiological studies on the topic of talc and ovarian cancer, noting that 63% show a positive association, while 37%, including the strongest cohort studies, show no association. In my opinion, the studies cited by this report are weak and unconvincing (see below).

There is no compelling evidence that talc causes ovarian cancer: Multiple lines of evidence are needed to convincingly show that a given agent is carcinogenic. These have been

standardized into specific criteria, known as the Bradford Hill criteria [46].

1. **Strength of association:** Multiple epidemiologic studies have investigated a possible relationship between talc and *any* type of ovarian cancer. As discussed above, it is not biologically meaningful to lump together all ovarian cancer subtypes, as they arise from different cells-of-origin, distinct genetic events and therefore, different types of DNA damage/repair problems. Even so, the epidemiological studies have been inconsistent, and the purported effects, even when present, are small. A recent “meta-analysis” (aggregate analysis) included 24 case-control and three cohort studies, and found an association between “any perineal use” of talc (including use on diaphragms and sanitary napkins) and ovarian cancer with an odds ratio (OR) of 1.31 [47]. When the entire meta-analysis was considered, risk was only increased for HGSOC and EC. Based on their distinct pathogenesis, however, it is not clear why only these two subtypes showed increased risk. In particular, as discussed above, CCC and EC arise in endometrial cells and have similar mutational spectra. It is unclear why one, but not the other, would show an increase, if women were exposed to the same pro-cancer agent. Similar conclusions were reached in meta-analyses by Berge *et al.* [48], and by the aforementioned Health Canada review [45].

Notably, cohort studies fail to find an increased risk of ovarian cancer overall with “any use” of talc. In their meta-analysis, Berge *et al.* [48] note that, based on the combined number of cases and controls in the cohort studies, the statistical power to detect an association in these studies, when pooled, should have been 99%. The pooled cohort studies do report a small increase in HGSOC for ever use of talc (OR 1.25). This increase is quite small, though; by comparison, smoking causes a 25-fold increase in risk of lung cancer. (See Smoking and Cancer, https://www.cdc.gov/tobacco/data_statistics/sgr/50thanniversary/pdfs/fs_smoking_cancer_508.pdf.) When an effect is so small, it is difficult to rule out other potential contributors to ovarian cancer, or HGSOC, risk. For example, a major weakness of all of these studies is that the talc exposures are self-reported, and therefore accurate quantification of exposure is difficult. Also, exposures occurred via different routes, and the various studies did not find that routes of exposure were equivalent. Alternatively, some other practice or exposure that is not routinely queried might be more common in talc users. Furthermore, none of these studies restricted themselves to the products at issue in this litigation (Johnson’s Baby Powder and Shower to Shower), and therefore any conclusion about the products at issue is inherently confounded.

2. **Consistency of Relationship:** As noted above, the individual epidemiologic studies do not show a consistent relationship between talc and ovarian cancer, and the meta-analyses show differences between the population-based case-control studies and the cohort studies. The case-control design attempts, as best as possible, to match cases to individuals who share the same characteristics except the disease under study. However, because a patient knows she has the disease, case-control studies can be confounded by “recall bias.” For example, if news reports indicate a possible connection between talc exposure and ovarian cancer, recollections can be different. The finding of a higher relative risk in more recent case-control studies, compared with earlier ones [49, 50], is consistent with this potential problem, as noted by Berge *et al.* [48]. In the latter study, for example, an association with “ever use” was only seen for patients interviewed after 2014, when there was already substantial

publicity about a potential talc/ovarian cancer connection. The authors of the study explicitly acknowledge the possible influence of litigation, but nevertheless, such influence seriously confounds any conclusion that talc caused the ovarian cancers seen in these women. Also unclear is why hospital-based case-control studies fail to detect an association whereas population-based reports do detect one, again suggesting that these studies might not be capturing all relevant variables [45, 48, 51]. The case-control studies also are inconsistent regarding exposure route. Some see an increase in ovarian cancer incidence in women exposed by “any route” [50, 52]. Notably, exposure via talc on condoms or diaphragms, which one might expect to introduce particles to the upper genitourinary (GU) tract (i.e., the area of the body encompassing the reproductive organs) more proximately than perineal dusting, did not show increased risk when queried [45, 47, 48]. Also, different studies are heterogeneous regarding the source of talc, the inclusion or exclusion of other powders, other queries about other potential confounding factors (e.g., douching [53]) and the extent of genetic risk data collected [45].

3. **Biological Plausibility:** For an agent to be adjudged the cause of cancer, there must be a demonstration of a plausible biochemical mechanism. In my opinion, there simply are no compelling data to this effect. As noted above, talc is universally acknowledged to be non-genotoxic in standard mutagenesis assays. The plaintiffs’ experts cite several alternative mechanisms by which talc could be cancer-promoting, but the evidence supporting each of these mechanisms is quite weak, as detailed below:

Route of access: The plaintiffs’ experts argue that talc can be transported from the vagina through the cervix to the uterus and into the fallopian tube, ovary and peritoneum. No data are available relating perineal exposure to exposure in the relevant target tissue. It simply is not clear whether talc can regularly get from the perineal area to the region of the fallopian tube or the ovarian surface epithelium, and even if it can, the relationship between the amount of talc applied to underwear or sanitary napkins and the amount that reaches the relevant cells is completely unclear. The plaintiffs’ experts do not identify any convincing, direct evidence on this point. Instead, they cite to earlier papers to support this hypothetical possibility. For example, Egli and Newton [54] placed inert dextran particles via a speculum into the posterior fornices of the vagina of three women undergoing elective hysterectomy (and thus under general anesthesia). They then administered 10U of oxytocin, rapidly placed the patient in the supine, flat position, retrieved the fallopian tubes, and found particles in 2/3 within 28-34 min. It should be obvious that the design of this study bears little resemblance to the standard ways that women use talc in the perineal area. Furthermore, the above study is seriously compromised by its small size, use of anesthesia and oxytocin (which causes uterine contractions), and lack of information regarding the relative dose of these particles compared to what might be reasonably expected to be a dose of talc from perineal dusting. These authors argue for the physiological relevance of the oxytocin administration, as oxytocin is released during intercourse. In that case, one might expect that talc on diaphragms or on condoms would show the largest association with risk in the epidemiological studies. However, as mentioned above, the epidemiological studies find exactly the opposite. Venter and Iturralde [55] deposited radioactively labelled albumin microspheres into the posterior fornices of 24 patients one day before different operations. Only 21 cases could be examined (in the other, the particles streamed out of the vagina), and

16 showed radioactivity reaching the uterus or higher. This study is also compromised by a lack of clear relevance between depositing large numbers of particles in the posterior fornix versus perineal dusting of talc.

By contrast, Heller *et al.* [56] examined the ovaries of 24 women undergoing incidental oophorectomy, and collected data on talc use. Twelve women reported frequent perineal talc application; the other 12 reported no use. Blocks of ovarian tissue were digested and examined by polarized light microscopy and electron microscopy. Talc was detected in all 24 patients, regardless of exposure. Although these data show that talc can be found at high frequency within ovarian tissue, they argue strongly that perineal talc use does not accurately reflect potential exposure. Similarly, Henderson [57] found talc in 10/13 ovarian tumors, 12/21 cervical tumors, and 5/12 normal ovaries. There was no correlation between particle count and patient-reported talc exposure. Together, these findings, which would appear to be directly on-point, vividly illustrate the unreliability of conclusions based solely on epidemiological studies that rely entirely on self-reporting of talc exposure. Furthermore, no evidence of inflammation, fibrosis or other forms of damage to the ovaries or FT was reported by either Heller *et al.* or Henderson.

Purported carcinogenic mechanism: Talc is not genotoxic in standard mutagenicity assays in lower organisms, has never been shown to induce mutations in any cancer-causing gene (oncogene or TS gene) in human cells, and has not been shown to cause CNAs in any setting. Plaintiffs' expert, Dr. Saed, argues that talc promotes cancer by inducing oxidative stress, which in turn could be mutagenic. He provides several potential mechanisms by which this could occur, much of it based on his own work. In my opinion, these studies are technically and conceptually flawed, and do not withstand critical scrutiny. I will discuss each of these claims below:

- a) “[O]varian cancer patients manifest significantly decreased levels of antioxidants and higher levels of oxidants” (p. 5). Regardless of whether this statement is true, it is a *non-sequitur* insofar as ovarian cancer pathogenesis is concerned. By the time a patient has developed obvious ovarian cancer, one cannot determine whether the above phenomena are cause or effect. Dr. Saed provides no evidence on the oxidation state of *pre-malignant* lesions, which is when a carcinogen that promotes inflammation would be expected to act.
- b) “MPO . . . and iNOS . . . are highly expressed and co-localized . . . in EOC cells” (p. 5). Again, even if this statement were true, it too is a *non-sequitur*, for the reasons discussed above. Indeed, the claim that MPO is not expressed in normal ovarian epithelium, if anything, argues against any purported involvement in talc-mediated ovarian carcinogenesis. I have reviewed the paper that Dr. Saed quotes (from his own laboratory) to support this claim, and find it seriously flawed at multiple levels. First, he uses one cell line (SKOV3) that is not representative of HGSOC [58] and another of uncertain provenance. Since the focus of many of plaintiffs' experts is on the potential association between talc and HGSOC, which is also the most common form of ovarian cancer, these cell lines are irrelevant. Second, he uses immunostaining methods to identify MPO, but fails to provide key controls for his reagents. This shortcoming is no trivial matter, given

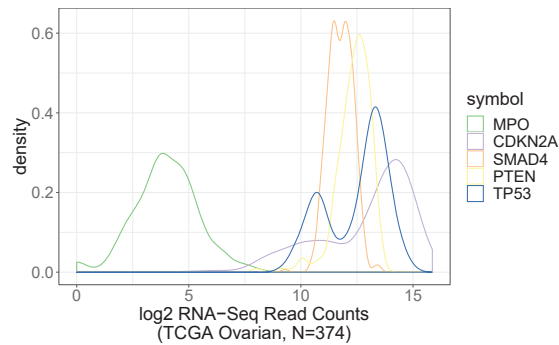


Figure 1: RNA-sequencing counts for *MPO*, compared with known ovarian cancer TS genes, showing virtually undetectable expression of the former in 374 HGSOC. Raw data available at: www.portal.gdc.cancer.gov.

that *MPO* is only known to be expressed in myeloid cells, and inspection of the Cancer Cell Line Encyclopedia (CCLE) database (<https://portals.broadinstitute.org/ccle>) reveals no significant *MPO* mRNA expression in cell lines other than those of myeloid origin. Likewise, inspection of The Human Cancer Genome Atlas data on HGSOC shows that *MPO* RNA is virtually undetectable; notably, its levels are lower than those of standard ovarian cancer TS genes (Figure 1). Most likely, the low residual counts reflect *MPO* expression in infiltrating myeloid cells rather than, as claimed by Dr. Saed, tumor cell expression. Third, his functional

experiments, involving a technique known as RNA interference (RNAi), lack standard controls. In RNAi experiments, scientists introduce short double stranded sequences (siRNAs) into cells. These siRNAs can direct the degradation of mRNAs that contain this sequence, but the technique is not absolutely specific. Instead, a given siRNA can gratuitously degrade other mRNAs, a phenomenon we term “off-target” effects. All high-quality journals require that such controls be performed; yet, they were not done in Dr. Saed’s paper.

- c) “Common SNPs in the redox enzymes are known to be strongly associated with altered enzymatic activity . . . that has been linked to . . . ovarian cancer” (p. 7-8). It is true that a SNP in *GPX6*, which encodes a redox enzyme, is associated with HGSOC risk, although notably, Dr. Saed does not mention this SNP. The ones that he does discuss either do not reach genome-wide significance (and thus are not conclusively associated with ovarian cancer risk) or are associated with other biological processes. **See Appendix A.** For example, the only SNPs in the catalase gene (*CAT*) that reach genome-wide significance affect blood catalase levels, whereas *MPO* SNPs are associated with blood levels of this enzyme or with white blood cell levels (<https://www.ebi.ac.uk/gwas/genes/MPO>). **See Table 1 (adapted from <https://www.ebi.ac.uk/gwas/search?query=mpo>).**

**Table 1 – GWAS Associations For *MPO* That Reach Genome-Wide Significance
(Note Lack of Ovarian Carcinomas)**

Disease/Trait	Region	Reported Gene	Mapped Gene	Source
Circulating myeloperoxidase levels (plasma)	17q22	<i>MPO</i> , <i>RNF43</i> , <i>PPM1E</i>	<i>MPO</i> - <i>BZRAP1</i>	Reiner AP. Genome-wide and gene-centric analyses of circulating myeloperoxidase levels in the charge and care consortia. <i>Hum Mol Genet.</i> 2013 Aug 15;22(16):3381-93.

Disease/Trait	Region	Reported Gene	Mapped Gene	Source
Blood protein levels	17q22	NR	MPO	Sun BB. Genomic atlas of the human plasma proteome. Nature. 2018 Jun;558(7708):73-79.
Blood protein levels	17q22	NR	MPO	Sun BB. Genomic atlas of the human plasma proteome. Nature. 2018 Jun;558(7708):73-79.
Blood protein levels	17q22	MPO	MPO - BZRAP1	Sun BB. Genomic atlas of the human plasma proteome. Nature. 2018 Jun;558(7708):73-79.
Post bronchodilator FEV1/FVC ratio in COPD	17q22	MPO	MPO	Lutz SM. A genome-wide association study identifies risk loci for spirometric measures among smokers of European and African ancestry. BMC Genetics 2015 16:138.
Monocyte count	17q22	MPO	MPO - BZRAP1	Astle WJ. The Allelic Landscape of Human Blood Cell Trait Variation and Links to Common Complex Disease. Cell. 2016 Nov 17;167(5).
Monocyte percentage of white cells	17q22	MPO	MPO - BZRAP1	Astle WJ. The Allelic Landscape of Human Blood Cell Trait Variation and Links to Common Complex Disease. Cell. 2016 Nov 17;167(5).
Granulocyte percentage of myeloid white cells	17q22	MPO	MPO - BZRAP1	Astle WJ. The Allelic Landscape of Human Blood Cell Trait Variation and Links to Common Complex Disease. Cell. 2016 Nov 17;167(5).
Neutrophil percentage of white cells	17q22	MPO	MPO	Astle WJ. The Allelic Landscape of Human Blood Cell Trait Variation and Links to Common Complex Disease. Cell. 2016 Nov 17;167(5).
Myeloid white cell count	17q22	MPO	MPO	Astle WJ. The Allelic Landscape of Human Blood Cell Trait Variation and Links to Common Complex Disease. Cell. 2016 Nov 17;167(5).
Granulocyte	17q22	MPO	MPO	Astle WJ. The Allelic Landscape of

Disease/Trait	Region	Reported Gene	Mapped Gene	Source
count				Human Blood Cell Trait Variation and Links to Common Complex Disease. Cell. 2016 Nov 17;167(5).
Sum neutrophil eosinophil counts	17q22	MPO	MPO	Astle WJ. The Allelic Landscape of Human Blood Cell Trait Variation and Links to Common Complex Disease. Cell. 2016 Nov 17;167(5).
Sum basophil neutrophil counts	17q22	MPO	MPO	Astle WJ. The Allelic Landscape of Human Blood Cell Trait Variation and Links to Common Complex Disease. Cell. 2016 Nov 17;167(5).
Neutrophil count	17q22	MPO	MPO	Astle WJ. The Allelic Landscape of Human Blood Cell Trait Variation and Links to Common Complex Disease. Cell. 2016 Nov 17;167(5).
White blood cell count	17q22	MPO	MPO	Astle WJ. The Allelic Landscape of Human Blood Cell Trait Variation and Links to Common Complex Disease. Cell. 2016 Nov 17;167(5).

Furthermore, the fact that alterations in redox state might contribute to ovarian cancer risk implies nothing about whether talc is oncogenic; nor does it imply that talc is in any way associated with redox state in the fallopian tube or ovarian surface epithelium.

- d) “*Chemoresistance is Associated with Point Mutations in Key Redox Enzymes in EOC cells*” (p. 9). Again, this entire line of reasoning is not germane to the issue of talc and ovarian cancer. Also, HGSOC is a disease of CNAs, not point mutations (see above).
- e) “[T]alc . . . initiates a[n] . . . inflammatory response” (p. 10/11). There simply is no compelling evidence that talc induces an inflammatory response in the female genital tract. Notably, no evidence of inflammation was reported in studies that documented talc in surgical tissue from women undergoing oophorectomy (see above). In other words, when the putatively offending substance has been found in the site in which ovarian cancer develops, there have been no evident pro-inflammatory *effects*!
- f) “*Studies that exposed lab animals (rats, mice, hamsters) to asbestos-free talcum powder in various ways have had mixed results*” (pp. 10-11). Here, it is unclear to what Dr. Saed is referring, as he cites two epidemiology papers, not biology experiments. ***In fact, no***

animal studies have shown that ovarian cancer develops following talc injection.

- Hamilton *et al.* [59] injected talc directly into the rat ovarian bursa (the junction of the FT and the ovary). *They specifically noted that no malignancies were observed.* They also did not report evidence of STIC, the well-accepted precursor lesion for HGSOV, as discussed above. Focal papillary changes were seen in the OSE, but the authors noted that these changes could be due to high concentrations of hormones that accumulated in the intrabursal space due to the amount of talc injected. They also specifically noted *no evidence of inflammation*, although foreign body granulomas were seen. Importantly, granulomas are *not* observed during human ovarian cancer development (e.g., in patients with STICs). Moreover, the doses that were injected were massive (100 ul of 100 mg/ml talc suspension). The authors concluded that their results were “preliminary,” and notably, they never published on this topic again. Nevertheless, the fact that these massive amounts of talc failed to show any evidence of pro-oncogenic effects is strong evidence against plaintiffs’ experts’ arguments.
 - Keskin *et al.* [60] delivered talc to rats intravaginally or via their perineum. They also observed foreign body reactions (granulomas), as well as infections, in both groups exposed to talc, but *no neoplastic changes*. They concluded that talc causes foreign body reaction and infection, but not cancer.
- g) “*Migration/transport of particles through the genital tract is universally accepted*” (p. 11). Again, as discussed above, the evidence supporting this notion is far from “universally accepted”; to the contrary, it is actually quite limited. Furthermore, this mechanism fails to explain the frequent finding of talc particles in normal ovaries of women with no self-reported talc exposure. In its report evaluating the potential carcinogenicity of talc, IARC specifically noted that the evidence for transport was weak [44], whereas the recent Health Canada study maintained that data on talc migration were “inconsistent [45].”
- h) “[T]he inflammatory nature of talcum powder [is] consistently demonstrated” (p. 11). Notwithstanding this strong statement, the evidence simply fails to support this claim. As noted above, injection of large amounts of talc into the relevant organs in experimental animals does NOT cause inflammation other than granulomas, much less neoplasia. Similarly, there is no evidence of any type of inflammation – including granulomas – in women with documented talc particles in their ovaries (see above). Dr. Saed cites a paper by Shukla *et al.* [61] in which human mesothelial cells were exposed to talc for eight and 24 hours, respectively, and some changes in *gene expression* were noted. This study examines a cell type (immortalized pleural mesothelial cells) that is not directly relevant to ovarian cancer pathogenesis, and even then, reports quite minor changes in gene expression. The same study included limited studies on immortalized OSE cells, but found almost no significant changes in gene expression. As discussed above, OSE also is likely not to be the target cell for most HGSOV, and even if it were, there is no evidence that talc causes anything other than granulomas, which are not typically associated with

human ovarian cancer and are seen in animals only at exceedingly high doses of talc instillation.

- i) “*Findings from recent research from [the Saed] laboratory*” (p. 13). Dr. Saed provides a manuscript in press and several abstracts purporting to show changes in the levels of certain redox enzymes in response to talc exposure, including exposure to Johnson’s Baby Powder. Even if one were to accept these data at face value, the mere finding of differences in the levels of certain redox enzymes does not alone provide evidence of an altered redox state within cells, much less a pro-oncogenic effect of talc. Notably, Dr. Saed fails to carry out standard measurements to assess intracellular ROS and/or their effects, such as DCF fluorescence (to measure H₂O₂ levels), BODIPY staining (to assess lipid peroxidation) or measurement of 8-oxo-dG in DNA (measurement of oxidative DNA damage). Also, these short-term assays in no way model what he claims throughout his report to be “chronic inflammation” induced by talc. It bears repeating that experimental animals and, most importantly, women, with documented talc exposure show no neoplastic changes, nor is there any evidence that talc evokes changes in redox state *in vivo*. Furthermore, it should be noted that careful examination of Dr. Saed’s laboratory notebooks reveals inconsistencies with the data in his abstract and manuscript, whited out sections, removal of some data points as “outliers” for unclear reasons, and the use of single biological replicates for each of the talc doses tested.
- j) In his manuscript, Dr. Saed also makes the truly extraordinary claim that “talc treatment was associated with a genotype switch” for SNPs in redox enzymes (Manuscript p. 7, 11; Report p. 19). What this means is that a specific base in DNA (“letter” in the DNA code) is somehow specifically changed in nearly 100% of the cells treated with talc, an agent that he acknowledges is not directly genotoxic! Even if talc were mutagenic (i.e., capable of inducing changes in the DNA code) – for example, by generating DNA-damaging ROS – such damage would be random, not affecting a specific base that just happened to be part of a SNP. It would be totally unprecedented for any agent to cause a switch in genotype at a specific locus, and Dr. Saed not only provides no mechanism to explain this claim, he does not appear to recognize just how extraordinary such a claim would be. Of note, I inspected the printouts for the SNP analysis in Dr. Saed’s lab notebooks, and several are technically flawed, making it difficult to be confident of the allele (“letter”) assignment. He could have easily confirmed these assignments by direct Sanger sequencing of the DNA, but did not do so. Simply stated, the reference to “talc treatment-induced gene point mutations” is not credible.

Dr. Saed’s in-press manuscript was previously rejected at the (higher quality) journal *Gynecologic Oncology*. Reviewer 1 of the initial manuscript noted that the paper’s claim that “‘oxidative stress is a key mechanism to the initiation and progression of ovarian cancer’ is not supported by this investigation.” I share that view. Similarly, Reviewer 2 noted that, “their data do not show, despite the authors’ claim, any evidence that these cells are transformed (i.e., malignant).... Consequently, neither tumor initiation nor progression is documented in this study, as opposed to the statement in Highlight #1 (in the text) and elsewhere. While changes in redox potential play an important role in tumor biology in general, the present data are insufficient to back up the claim that talcum (sic)

is central to the development of ovarian cancer.” I also share Reviewer 2’s view.

- k) Dr. Saed’s deposition testimony contains several statements that call into question his knowledge of basic cancer cell biology, genetics and biochemistry. For example, he states that p53 is an oncogene, whereas it is a paradigmatic tumor *suppressor* gene (p. 230). He states that cells are grown at normal oxygen and glucose levels (pp. 252-257), whereas in fact, they are typically grown at ~3X normal oxygen levels and 4X normal glucose concentrations. He does not appear to know that GWAS aggregates all published work on SNPs associated with disease risks and traits (pp. 205-206). His comments on SNPs in the catalase gene (p. 206-207) call into question his understanding of linkage disequilibrium, the concept that blocks of SNPs located close together in the genome are typically co-inherited. He does not appear to understand that the BCA assay is a colorimetric assay, rather than a direct measurement of absorbance (pp. 119-120). He does not seem to be aware of recent evidence that full-blown cancers are often more sensitive to oxidative stress [12]; indeed, one therapeutic approach under investigation in several laboratories is to promote increased oxidative stress in cancer cells. He states that CA125 is a marker of inflammation (p. 248), but this statement too is speculative. He states that normal cells have a higher apoptotic rate than cancer cells. Healthy normal cells do not have a higher apoptotic rate than cancer cells, although unhealthy or damaged normal cells are more likely to undergo apoptosis than cancer cells. Perhaps most importantly, none of Dr. Saed’s contentions or conclusions is based on animal studies, much less on human data.
- l) *Relationship between MUC1 antibodies and ovarian cancer pathogenesis (Zelikoff report, p. 19).* Plaintiffs’ expert Dr. Judith Zelikoff cites work showing that talcum powder users have lower plasma levels of MUC1 antibodies than non-users [62], and proposes that decreased immunity to MUC1 could be a mechanism by which talc increases ovarian cancer risk. Anti-tumor immunity is primarily mediated by anti-tumor T lymphocytes and possibly NK cells [63]. Because there is no evidence that anti-MUC1 antibodies (which are produced by B-lymphocytes) play any role in immune surveillance of ovarian or other types of cancer, this opinion should be viewed as pure speculation.
- m) *“Recent clinical and prospective data suggest that C-reactive protein (CRP), a marker of global inflammation, is associated with increased ovarian cancer risk” (Zelikoff, p. 20).* Dr. Zelikoff cites work by Poole [64], who measured the association of various inflammatory markers and ovarian cancer development in the Nurse’s Health Studies 1 and 2 and the Women’s Health Study (WHS). This study showed a 53% increase in risk for ovarian cancer for women with the highest (4th) quartile, compared with the lowest (1st) quartile, CRP levels in the blood. Notably, there was no association with IL6 (a cytokine marker of inflammation) or secreted TNF α R2 levels (another inflammatory marker). This study, as well as work by Trabert *et al.* [65], shows that some degree of systemic inflammation may be present during the development of ovarian cancer. However, a recent analysis of 26 STIC and early serous carcinomas saw no evidence of inflammation [66]. Moreover, NHS-1 and the WHS collected talc exposure data – indeed, these are among the major cohort studies of the talc/ovarian cancer association. Yet, while they could have addressed this key question, neither Poole *et al.* nor Trabert *et al.*

analyzed the relationship between perineal talc exposure and inflammation. Hence, there simply is no evidence in these papers that links perineal talc exposure to inflammation, whereas, as mentioned above, direct experiments argue against any such link. It also remains possible that increased CRP is a sign of inflammation that results from, rather than causes, ovarian cancer, a possibility acknowledged by Poole *et al.* Notably, a subsequent meta-analysis of this issue concluded that “Further studies are needed to definitively identify the role of CRP in the etiology of ovarian cancer [67].”

n) *Effect of talc on macrophages and relevance to ovarian cancer.* In her report, Dr. Zelikoff (pp. 22-24) raises the possibility that talc ingestion, either directly or on lipid particles, might have pro-inflammatory effects on macrophages. In fact, the picture that emerges from the papers she cites is complex, confusing and in some cases contradictory. In no way does the evidence cited by Dr. Zelikoff rise to the level of scientifically conclusive.

- **Bogatu and Contag** [68] argue that talc binds to high-density lipoprotein particles, which are then ingested into macrophages. Dr. Zelikoff notes that this could trigger a fibrogenic reaction (scar formation). However, there is no evidence for the involvement of scarring/fibrosis in ovarian carcinogenesis. Furthermore, there was no evidence of scarring in ovaries in which talc particles were detected. Indeed, Bogatu and Contag’s focus was on mechanisms underlying silicosis, not ovarian cancer.
- **Ghio *et al.*** [69] report that mineral talc sequesters iron (Fe) from cells, resulting in increased Fe uptake, oxidative stress and ROS production. This study involved immortalized bronchial epithelial and primary pleural mesothelial cells, which are not obviously relevant to ovarian cancer. Furthermore, there is no evidence that injecting talc into the pleural space causes lung cancer or mesothelioma.
- **Akhtar *et al.*** [70, 71] measured the effects of talc on A549 cells, and found ROS production, oxidation of cellular lipids and DNA damage. The relevance of this work to ovarian carcinogenesis also is extremely questionable. Because A549 are lung cancer cells, they are from an irrelevant cell-of-origin and are already malignant. In addition, it is not clear how the doses seen here relate to the small number of particles in the female reproductive tract.
- **Davies *et al.*** [72] studied the effects of seven specimens of respirable talc dust on mouse peritoneal macrophages, and observed mild, but consistent, cytotoxicity and suggested that talc could be fibrogenic. Again, there is no evidence that fibrosis plays a role in ovarian cancer pathogenesis.
- **Hamilton *et al.*** [73], on the other hand, found that talc caused a small *increase* in the proliferation of mouse bone marrow-derived macrophages (the opposite of the effects seen by Davies *et al.* on peritoneal macrophages). At higher doses, toxicity was observed, however. Based on these data, they argue that talc could cause granulomas. Indeed, granulomas were seen in the talc injection studies noted

above, but granulomas are not seen in women who have talc particles in their ovaries or as part of ovarian carcinogenesis.

o) Effect of talc on ovarian surface epithelial cells. Several of plaintiffs' experts (including Dr. Zelikoff) cite work by Buz'Zard and Lau [74] as evidence that talc is pro-oxidative and causes transformation of ovarian cells. This paper examined the effects of talc on immortalized human ovarian granulosa (GC1a) cells, immortalized human ovarian surface epithelial (OSE2a) cells and primary human polymorphonuclear leukocytes (PMNs; PMNs, also known as neutrophils, are the major white blood cell in human peripheral blood). The authors claimed that talc increased cell viability (cell number) of OSE2a and GC1a cells at low doses, but decreased it at higher doses (>200 ug/ml). They also claim that it increased the growth of these cell lines in soft agar at 5ug/ml and 20 ug/ml. At low doses, talc decreased ROS generation in OSE2a and increased ROS in GC1a cells, while decreasing ROS at higher talc concentrations in OSE2a cells. Finally, they find that talc causes increased ROS generation in PMNs across a broad dose range. In my opinion, this study, and its interpretation by plaintiffs' experts, is seriously flawed, for multiple reasons:

- The talc was obtained from a standard chemical reagent company, Sigma, and its quality, mineral and/or fibrous content and composition were not assessed.
- Granulosa cells are totally irrelevant to the study of epithelial ovarian carcinoma, meaning that the experiments with GC1a cells are not germane to the plaintiffs' case.
- OSE2a cells are a single, immortalized cell line, produced by transformation of normal OSE from a single woman of reproductive age with large T antigen of SV40. The use of these cells as a model for the early events of ovarian carcinogenesis is problematic on multiple levels. First, normal OSE is not the cell-of-origin for most ovarian cancer. Second, large T antigen is a viral gene product that evokes changes equivalent to at least two of the transformation events needed for ovarian carcinogenesis. Third, large T-transformed cells are genetically unstable, and no two cells transformed in this way are the same. Hence, this choice of cell system is inapt for studying mechanisms of ovarian carcinogenesis.
- Notwithstanding the choice of experimental system, the effects on proliferation are very small, quite dose-sensitive, and not likely to be biologically relevant.
- Of note, the purported pro-oncogenic effects on proliferation and ROS occur at two different doses of talc. As noted several times above, it is difficult to know what would be an appropriate dose to model the supposed level of talc in the GU tract of women exposed to perineal dusting powder.
- Growth in soft agar does not mean tumorigenicity – at least not with human cells, and as with the growth effects, at higher concentration, soft agar colony formation

is eliminated by talc treatment.

- The relevance of the PMN experiments is not clear. No role for neutrophils in ovarian carcinogenesis has been suggested by plaintiffs' experts, much less demonstrated experimentally.

- p) *Effect of talc on CA125 levels.* (p. 25) Dr. Zelikoff cites work by plaintiffs' expert Dr. Saed (discussed above) that talc induces the expression of the cancer antigen CA125 in normal ovarian cells and ovarian cancer cells. Even if these observations are true, there is no obvious relevance to ovarian cancer pathogenesis. As Dr. Zelikoff notes, CA125 is a "biomarker" for ovarian cancer detection, but it has no known role in ovarian cancer *causation*. Whether or not talc induces CA-125 expression says nothing about talc having any carcinogenic effect. Notably, in her deposition (p. 352), Zelikoff states that CA125 is MUC1. CA125 is, however, MUC16, raising the possibility that she is confusing these two proteins.
- q) *Effect of talc on expression of redox enzymes.* Dr. Zelikoff also cites "[e]merging science" (p. 25) from the Saed laboratory claiming that talc treatment of ovarian cancer cell lines and normal ovarian cells causes changes in the levels of mRNA for multiple pro-oxidant and anti-oxidant genes. The multiple problems with this work have been detailed above. Also, in her deposition (p. 236), Dr. Zelikoff states that talc leads to changes in gene expression, which "can be inferred as a mutation." This statement is categorically incorrect – changing the media on cells can cause changes in gene expression. Changing temperature can change gene expression. In no way can one "infer" a mutation merely because gene expression is altered.
- r) *Women with certain genetic variants have increased risk of ovarian cancer with talc use.* Dr. Zelikoff (p. 26) points to epidemiological data from Gates *et al.* [75] who carried out a case-control study genotyping SNPs in *GSTM1*, *GSTT1* and *NAT2* in participants from the New England based Case-Control and Nurses Health studies. The authors found that these SNPs were not themselves associated with risk, but the association of ovarian cancer with talc use was stronger in women with the GST-null genotype, and further enhanced in women with the *GST1-null* and *GSTM1-present*. The study concludes that "women with certain genetic variants may have a higher risk of ovarian cancer associated with talc use." However, the authors also specifically stated that "...additional research is needed to confirm these findings and to explore potential mechanisms for these interactions...." There appears to have been no subsequent follow up/confirmation of these data. Given that positive results are nearly always published, whereas negative results often are not (a phenomenon termed "publication bias"), it seems likely that these observations are not reproducible (or the authors would have published a subsequent paper verifying the association). Also, it should be noted that no biological/biochemical mechanism is available to explain why a higher level of *GSTM1* and a lower level of *GST1* increase interaction with talc, as these enzymes both catalyze the same biochemical reaction

Several additional lines of evidence argue against the “talc-induced inflammation model” of ovarian carcinogenesis proposed by the authors, most which have been cited above. First and foremost, whereas the evidence cited by plaintiffs’ experts is indirect, involves irrelevant cell lines, and/or is not definitive, the most direct evidence available contradicts their argument. As noted, injection of talc directly into the ovarian bursa of animals does NOT evoke inflammation, much less cancer. Similarly, women with talc particles in their ovaries do not show evidence of inflammation. Nor am I aware of any publications that have reported finding STICs, the only known pre-neoplastic lesion in HGSOV, in women or animals with talc in their genitourinary tracts. Conversely, a recent study found “no significant correlation . . . between serous carcinoma and histological signs of inflammation or chronic tubal injury” [66]. Inflammatory diseases, such as rheumatoid arthritis, systemic lupus erythematosus, psoriatic arthritis, etc., are not known risk factors for ovarian cancer [43]. And finally, there is no consistent evidence that NSAIDs mitigate ovarian cancer risk [52, 76-83].

4. ***Consideration of Alternative Explanations:*** As with any weak epidemiologic association, the use of talc could be associated with other conditions that promote ovarian cancer. For example, women who use talc might be more likely to have a sub-clinical infection. Also, since the publication of these epidemiology studies, numerous additional strong risk genes for ovarian cancer have been identified, as have multiple weaker risk alleles. These were not tested in the patient populations used in these studies, and thus might not have been distributed equally in the talc and non-talc groups. In the case-control studies, recall bias is a major, demonstrable concern that has not been adequately eliminated. One of the major meta-analyses [48] found significant evidence of heterogeneity, complicating the conclusions that could be drawn. Heterogeneity means that the designs of the studies have so many differences that it might not be valid to combine them.
5. ***Dose-Response:*** An agent that has *bona fide* pro-oncogenic effects is expected to show increasing effect with increasing dose of the agent. Yet the epidemiologic data fail to show a compelling dose-response relationship.
 - None of the cohort studies reveals a dose-response relationship [53, 84-86].
 - Multiple case-control studies also fail to show evidence of a dose-response:
 - 1) Mills *et al.* [87] found essentially no difference in the odds ratio for the lowest and highest quartiles of cumulative exposure ((1.03 (0.59-1.80)) and (1.06 (0.62-1.83)), respectively) and concluded that “no dose response association was found.”
 - 2) Cook *et al.* [88] looked for an association across various strata of “cumulative lifetime days,” and saw no statistically significant elevated risk for any of the four categories.
 - 3) Meta-analyses and pooled studies have concluded that no clear, consistent dose-response relationship can be demonstrated; e.g., [45, 47, 48, 89, 90].

- 4) The National Cancer Institute and the FDA have concluded that a dose-response relationship has not been found. (Nat'l Cancer Inst., Ovarian, Fallopian Tube, and Primary Peritoneal Cancer Prevention (PDQ®)–Health Professional Version, <https://www.cancer.gov/types/ovarian/hp/ovarian-prevention-pdq> (last updated June 22, 2018); Letter from Food & Drug Admin., Dep't of Health & Human Servs., to Samuel S. Epstein, M.D., Cancer Prevention Coalition, University of Illinois - Chicago School of Public Health (Apr. 1, 2014).) The recent Health Canada analysis noted that “concerns that the actual exposure experienced by these women over the past 40-50 years is not well understood [45].”
 - 5) Some observational studies have argued for a dose-response relationship (e.g., [49, 50, 91], but these studies and their conclusions have significant issues. It is particularly difficult to retroactively quantify exposure. Also, exposure via diaphragms or condoms is not consistently associated with risk, even though such routes might be expected to provide the highest, and certainly the most direct, exposure. As noted above, proponents of talc transit have suggested that sexual activity facilitates exposure. In that case, one would expect talc on condoms or diaphragms to be particularly dangerous.
6. **Coherence:** A theory that an agent causes disease should be internally coherent and also fit with existing, accepted science. But plaintiffs' experts' theories do not satisfy this requirement. In particular, humans given high doses of talc in other body cavities (e.g., via pleurodesis) or exposed occupationally do not have increased cancer risk. Yet most of the pro-oncogenic mechanisms proposed by plaintiffs' experts would be expected to operate in multiple body sites. Nor does it make logical sense that talc use would cause multiple subtypes of ovarian cancer, which have different cells of origin, different types of mutations and mutational effects, and therefore likely different oncogenic mechanisms.

IV. CONCLUSIONS AND SUMMARY OF OPINIONS

Scientific support for the theory that talc use can cause ovarian cancer is lacking. The plaintiffs' experts' causation theories do not comport with what we know about carcinogenesis generally or the development of ovarian cancer specifically; nor do they have sufficient support from epidemiological research. In particular, Dr. Saed's work is rife with errors and overstated claims that betray a lack of understanding of cancer genetics – perhaps most notably his claim that talc induces specific point mutations in certain SNPs. Moreover, Dr. Saed's work, even if the significant errors, gaps and irregularities in his lab work are ignored, rests on a series of totally unsubstantiated assumptions, including the role (if any) of inflammation or oxidant states in ovarian cancer pathogenesis, the relevance (if any) of certain SNPs to ovarian cancer, and the significance (if any) of elevated CA-125 levels to ovarian carcinogenesis. More generally, the plaintiffs' experts' theories of biological mechanism lack support in the literature – indeed, if anything, existing literature tends to negate, rather than support, their proposed mechanism. Finally, evidence from the epidemiological literature shows only weak or nonexistent associations between talcum powder use and ovarian cancer and has failed to demonstrate any strong evidence of dose-response.

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Materials Considered

Expert Reports

- 2018.11.12 - Expert Report of Michael M. Crowley, PhD
- 2018.11.14 - Expert Report of William E. Longo, PhD & Mark W. Rigler, PhD
- 2018.11.15 - Expert Report of Sarah Kane, MD
- 2018.11.16 - Expert Report of Alan Campion, PhD
- 2018.11.16 - Expert Report of Anne McTiernan, MD PhD
- 2018.11.16 - Expert Report of April Zambelli-Weiner, PhD, MPH
- 2018.11.16 - Expert Report of Arch Carson, MD, PhD
- 2018.11.16 - Expert Report of Daniel L. Clarke-Pearson, MD
- 2018.11.16 - Expert Report of David Kessler, MD
- 2018.11.16 - Expert Report of Ellen Blair Smith, MD
- 2018.11.16 - Expert Report of Ghassan Saed, PhD
- 2018.11.16 - Expert Report of Jack Siemiatycki, MSc, PhD
- 2018.11.16 - Expert Report of Judith Wolf, MD
- 2018.11.16 - Expert Report of Judith Zelikoff, PhD
- 2018.11.16 - Expert Report of Laura Plunkett, PhD, DABT
- 2018.11.16 - Expert Report of Mark Krekeler, PhD
- 2018.11.16 - Expert Report of Patricia Moorman, MSPH, PhD
- 2018.11.16 - Expert Report of Rebecca Smith-Bindman, MD
- 2018.11.16 - Expert Report of Robert B. Cook, PhD
- 2018.11.16 - Expert Report of Shawn Levy, PhD
- 2018.11.16 - Expert Report of Sonal Singh, MD, MPH
- 2019.01.15 - Supp. Expert Report of William E. Longo, PhD & Mark W. Rigler, PhD
- 2019.01.17 - Addendum to the Expert Report of Mark Krekeler, PhD
- 2019.01.22 - Amended Expert Report of Robert B. Cook, PhD

Deposition Transcripts

- 2019.01.21 - Zelikoff, Judith Deposition Transcript
- 2019.01.23 - Saed, Ghassan Deposition Transcript
- 2019.02.14 - Saed, Ghassan Deposition Transcript

Internet Resources

- <https://cancer.sanger.ac.uk/cosmic>
- <https://www.ebi.ac.uk/gwas/>
- <http://biorxiv.org/cgi/content/short/481200v1>
- https://www.cdc.gov/tobacco/data_statistics/sgr/50th-anniversary/pdfs/fs_smoking_cancer_508.pdf
- <https://portals.broadinstitute.org/ccle>
- <https://www.ebi.ac.uk/gwas/genes/MPO>
- <https://www.cancer.gov/types/ovarian/hp/ovarian-prevention-pdq>
- https://ntp.niehs.nih.gov/ntp/roc/content/listed_substances_508.pdf

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Other

- Documents produced by Ghassan Saed
- Int'l Agency For Research On Cancer, World Health Org., *93 Monographs on the Evaluation of Carcinogenic Risks to Humans: Carbon Black, Titanium Dioxide, and Talc* (2010)
- Int'l Agency for Research on Cancer, World Health Org., *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, No. 100C: Arsenic, Metals, Fibres, and Dusts* (2012)
- Letter from Food & Drug Admin., Dep't of Health & Human Servs., to Samuel S. Epstein, M.D., Cancer Prevention Coalition, University of Illinois - Chicago School of Public Health (Apr. 1, 2014)
The Human Cancer Genome Atlas

APPENDIX A

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GWAS ASSOCIATIONS FOR OVARIAN CARCINOMAS
(NOTE LACK OF GENES INCLUDED IN SAED'S LAB WORK)

Region	Reported Gene	Mapped Gene	Disease/Trait	Source
9p22.2	NR	BNC2 - LOC105375983	Epithelial ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
3q25.31	NR	METTL15P1 - LINC00886	Epithelial ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
3q25.31	NR	METTL15P1 - LINC00886	High-grade serous ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
9p22.2	NR	BNC2 - LOC105375983	High-grade serous ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
3q25.31	NR	METTL15P1 - LINC00886	Serous invasive ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
9p22.2	NR	BNC2 - LOC105375983	Serous invasive ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
3q25.31	NR	METTL15P1 - LINC00886	Invasive epithelial ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
9p22.2	NR	BNC2 - LOC105375983	Invasive epithelial ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
10q26.13	FGFR2	FGFR2	Cancer (pleiotropy)	Fehring G. Cross-Cancer Genome-Wide Analysis of Lung, Ovary, Breast, Prostate, and Colorectal Cancer Reveals Novel Pleiotropic Associations. Cancer Res. 2016 Sep 1;76(17):5103-14.
3q25.31	NR	TIPARP	Ovarian cancer	Pharoah PD. GWAS meta-analysis and replication identifies three new susceptibility loci for ovarian cancer. Nat Genet. 2013 Apr;45(4):362-70, 370e1-2.

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9p22.2	NR	BNC2 - LOC105375983	Ovarian cancer	Pharoah PD. GWAS meta-analysis and replication identifies three new susceptibility loci for ovarian cancer. Nat Genet. 2013 Apr;45(4):362-70, 370e1-2.
3q25.31	NR	TIPARP	Ovarian cancer	Pharoah PD. GWAS meta-analysis and replication identifies three new susceptibility loci for ovarian cancer. Nat Genet. 2013 Apr;45(4):362-70, 370e1-2.
9p22.2	NR	BNC2 - LOC105375983	Ovarian cancer	Pharoah PD. GWAS meta-analysis and replication identifies three new susceptibility loci for ovarian cancer. Nat Genet. 2013 Apr;45(4):362-70, 370e1-2.
17q12	HNF1B	HNF1B	Cancer (pleiotropy)	Fehringer G. Cross-Cancer Genome-Wide Analysis of Lung, Ovary, Breast, Prostate, and Colorectal Cancer Reveals Novel Pleiotropic Associations. Cancer Res. 2016 Sep 1;76(17):5103-14.
19p13.11	NR	BABA M1 - ANKLE1	High-grade serous ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
8q24.21	NR	LINC00824	Epithelial ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
8q24.21	NR	LINC00824	Serous invasive ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
19p13.11	NR	BABA M1 - ANKLE1	Serous invasive ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
8q24.21	NR	LINC00824	High-grade serous ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
5p15.33	NR	TERT	Low-grade serous and serous borderline ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.

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17q21.3 1	NR	PLEKH M1	Epithelial ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
19p13.1 1	NR	BABA M1 - ANKLE 1	Epithelial ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
9p22.2	BNC2, LOC64857 0, CNTLN	BNC2 - LOC105 375983	Ovarian cancer	Song H. A genome-wide association study identifies a new ovarian cancer susceptibility locus on 9p22.2. Nat Genet. 2009 Sep;41(9):996-1000.
5p15.33	NR	TERT	Serous borderline ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
8q24.21	NR	LINC00 824	Ovarian cancer	Pharoah PD. GWAS meta-analysis and replication identifies three new susceptibility loci for ovarian cancer. Nat Genet. 2013 Apr;45(4):362-70, 370e1-2.
19p13.1 1	NR	BABA M1 - ANKLE 1	Invasive epithelial ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
17q21.3 2	NR	SKAP1	Epithelial ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
8q24.21	NR	LINC00 824	Low-grade serous and serous borderline ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
8q24.21	NR	LINC00 824	Invasive epithelial ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
12q13.1 3	KRT8	KRT8	Cancer (pleiotropy)	Fehring G. Cross-Cancer Genome-Wide Analysis of Lung, Ovary, Breast, Prostate, and Colorectal Cancer Reveals Novel Pleiotropic Associations. Cancer Res. 2016 Sep 1;76(17):5103-14.

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2q31.1	NR	HAGLR OS, HAGLR	Epithelial ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
2q31.1	NR	HOXD3	Epithelial ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
17q21.3 2	NR	SKAP1	Serous invasive ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
9p22.2	NR	BNC2 - LOC105 375983	Ovarian cancer in BRCA1 mutation carriers	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
2q31.1	NR	HAGLR OS, HAGLR	Serous invasive ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
19p13.1 1	NR	BABA M1	Ovarian cancer	Pharoah PD. GWAS meta-analysis and replication identifies three new susceptibility loci for ovarian cancer. Nat Genet. 2013 Apr;45(4):362-70, 370e1-2.
2q31.1	NR	HOXD3	Serous invasive ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
11q13.3	Intergenic	LOC105 369366 - LOC105 369367	Cancer (pleiotropy)	Fehring G. Cross-Cancer Genome-Wide Analysis of Lung, Ovary, Breast, Prostate, and Colorectal Cancer Reveals Novel Pleiotropic Associations. Cancer Res. 2016 Sep 1;76(17):5103-14.
2q31.1	NR	HOXD3	Invasive epithelial ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
2q31.1	NR	HAGLR OS, HAGLR	Invasive epithelial ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.

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Region	Reported Gene	Mapped Gene	Disease/Trait	Source
2q31.1	HOXD1, HOXD3	HAGLR	Ovarian cancer	Goode EL. A genome-wide association study identifies susceptibility loci for ovarian cancer at 2q31 and 8q24. Nat Genet. 2010 Oct;42(10):874-9.
17q21.3 2	NR	SKAP1	High-grade serous ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
17q21.3 1	NR	PLEKH M1	Invasive epithelial ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
17q21.3 1	NR	PLEKH M1	High-grade serous ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
2q31.1	NR	HAGLR OS, HAGLR	High-grade serous ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
17q23.2	BRIP1	BRIP1	Ovarian cancer	Rafnar T. Mutations in BRIP1 confer high risk of ovarian cancer. Nat Genet. 2011 Oct 2;43(11):1104-7.
2q31.1	NR	HOXD3	High-grade serous ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
17q21.3 2	NR	SKAP1	Invasive epithelial ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
5p15.33	NR	TERT	Serous invasive ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
8q24.21	NR	LINC00824	Serous borderline ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
8q24.21	MYC	LINC00824	Ovarian cancer	Pharoah PD. GWAS meta-analysis and replication identifies three new susceptibility loci for ovarian cancer. Nat Genet. 2013 Apr;45(4):362-70, 370e1-2.

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17q21.31	NR	PLEKH M1	Serous invasive ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
5q11.2	Intergenic	LOC101928448 - LOC105378979	Cancer (pleiotropy)	Fehring G. Cross-Cancer Genome-Wide Analysis of Lung, Ovary, Breast, Prostate, and Colorectal Cancer Reveals Novel Pleiotropic Associations. Cancer Res. 2016 Sep 1;76(17):5103-14.
5p15.33	NR	TERT	High-grade serous ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
*	NR	*	High-grade serous ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
13q13.1	BRCA2	BRCA2	Cancer	Fehring G. Cross-Cancer Genome-Wide Analysis of Lung, Ovary, Breast, Prostate, and Colorectal Cancer Reveals Novel Pleiotropic Associations. Cancer Res. 2016 Sep 1;76(17):5103-14.
*	NR	*	Epithelial ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
10p12.31	NR	MLLT10	Epithelial ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
2q31.1	NR	HAGLR	Ovarian cancer	Pharoah PD. GWAS meta-analysis and replication identifies three new susceptibility loci for ovarian cancer. Nat Genet. 2013 Apr;45(4):362-70, 370e1-2.
9p22.2	cHMP4C, FABP5, PMP2, FABP12, IMPA1, SLC10A5, ZFAND1, SNX16, FABP4	BNC2 - LOC105375983	Ovarian cancer in BRCA1 mutation carriers	Couch FJ. Genome-wide association study in BRCA1 mutation carriers identifies novel loci associated with breast and ovarian cancer risk. PLoS Genet. 2013;9(3):e1003212.

APPENDIX A
GWAS ASSOCIATIONS FOR OVARIAN CARCINOMAS
(NOTE LACK OF GENES INCLUDED IN SAED'S LAB WORK)

Region	Reported Gene	Mapped Gene	Disease/Trait	Source
*	NR	*	Serous invasive ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
9p22.2	NR	BNC2 - LOC105375983	Ovarian cancer in BRCA2 mutation carriers	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
4q24	Intergenic	LOC100288146 - TET2	Cancer (pleiotropy)	Fehringer G. Cross-Cancer Genome-Wide Analysis of Lung, Ovary, Breast, Prostate, and Colorectal Cancer Reveals Novel Pleiotropic Associations. Cancer Res. 2016 Sep 1;76(17):5103-14.
5p15.33	TERT	TERT	Cancer (pleiotropy)	Fehringer G. Cross-Cancer Genome-Wide Analysis of Lung, Ovary, Breast, Prostate, and Colorectal Cancer Reveals Novel Pleiotropic Associations. Cancer Res. 2016 Sep 1;76(17):5103-14.
17q12	NR	HNF1B	Serous invasive ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
17q12	NR	HNF1B	Epithelial ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
14q24.1	RAD51B	RAD51B	Cancer (pleiotropy)	Fehringer G. Cross-Cancer Genome-Wide Analysis of Lung, Ovary, Breast, Prostate, and Colorectal Cancer Reveals Novel Pleiotropic Associations. Cancer Res. 2016 Sep 1;76(17):5103-14.
2q31.1	NR	HAGLR	Ovarian cancer	Pharoah PD. GWAS meta-analysis and replication identifies three new susceptibility loci for ovarian cancer. Nat Genet. 2013 Apr;45(4):362-70, 370e1-2.
17q21.32	NR	SKAP1	Ovarian cancer	Pharoah PD. GWAS meta-analysis and replication identifies three new susceptibility loci for ovarian cancer. Nat Genet. 2013 Apr;45(4):362-70, 370e1-2.

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GWAS ASSOCIATIONS FOR OVARIAN CARCINOMAS
(NOTE LACK OF GENES INCLUDED IN SAED'S LAB WORK)

Region	Reported Gene	Mapped Gene	Disease/Trait	Source
*	NR	*	Epithelial ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
1p36.33	Intergenic	DVL1 - MXRA8	Cancer (pleiotropy)	Fehring G. Cross-Cancer Genome-Wide Analysis of Lung, Ovary, Breast, Prostate, and Colorectal Cancer Reveals Novel Pleiotropic Associations. Cancer Res. 2016 Sep 1;76(17):5103-14.
13q13.1	BRCA2	BRCA2	Cancer (pleiotropy)	Fehring G. Cross-Cancer Genome-Wide Analysis of Lung, Ovary, Breast, Prostate, and Colorectal Cancer Reveals Novel Pleiotropic Associations. Cancer Res. 2016 Sep 1;76(17):5103-14.
12q24.31	NR	RPL12P33 - HNF1A-AS1	Epithelial ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
5p15.33	NR	TERT	Serous invasive ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
8q21.13	CHMP4C, FABP5, PMP2, FABP12, IMPA1, SLC10A5, ZFAND1, SNX16, FABP4	CHMP4C	Ovarian cancer	Pharoah PD. GWAS meta-analysis and replication identifies three new susceptibility loci for ovarian cancer. Nat Genet. 2013 Apr;45(4):362-70, 370e1-2.
5p15.33	NR	TERT	Invasive epithelial ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.

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(NOTE LACK OF GENES INCLUDED IN SAED'S LAB WORK)

Region	Reported Gene	Mapped Gene	Disease/Trait	Source
17q12	HNF1B, ACACA, C17orf78, TADA2A, DUSP14, SYNRG, DDX52, TBC1D3F, TBC1D3, MRPL45, GPR179, SOCS7, ARHGAP23	HNF1B	Ovarian cancer	Pharoah PD. GWAS meta-analysis and replication identifies three new susceptibility loci for ovarian cancer. Nat Genet. 2013 Apr;45(4):362-70, 370e1-2.
*	NR	*	Invasive epithelial ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
10p12.31	NR	MLLT10	Invasive epithelial ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
*	NR	*	High-grade serous ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
17q12	HNF1B	HNF1B	Cancer	Fehring G. Cross-Cancer Genome-Wide Analysis of Lung, Ovary, Breast, Prostate, and Colorectal Cancer Reveals Novel Pleiotropic Associations. Cancer Res. 2016 Sep 1;76(17):5103-14.
5p15.33	NR	TERT	Low-grade serous and serous borderline ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
1p34.3	NR	RSPO1	Epithelial ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.

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(NOTE LACK OF GENES INCLUDED IN SAED'S LAB WORK)

Region	Reported Gene	Mapped Gene	Disease/Trait	Source
3p24.1	NEK10	NEK10	Cancer (pleiotropy)	Fehring G. Cross-Cancer Genome-Wide Analysis of Lung, Ovary, Breast, Prostate, and Colorectal Cancer Reveals Novel Pleiotropic Associations. Cancer Res. 2016 Sep 1;76(17):5103-14.
19p13.1 1	BABAM1	BABA M1 - ANKLE 1	Cancer (pleiotropy)	Fehring G. Cross-Cancer Genome-Wide Analysis of Lung, Ovary, Breast, Prostate, and Colorectal Cancer Reveals Novel Pleiotropic Associations. Cancer Res. 2016 Sep 1;76(17):5103-14.
*	NR	*	Serous invasive ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
8q21.13	NR	LINC01 111	Low-grade serous and serous borderline ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
8q24.21	NR	PVT1	Epithelial ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
20q11.2 2	Intergenic	RPS2P1 - ASIP	Cancer	Fehring G. Cross-Cancer Genome-Wide Analysis of Lung, Ovary, Breast, Prostate, and Colorectal Cancer Reveals Novel Pleiotropic Associations. Cancer Res. 2016 Sep 1;76(17):5103-14.
8q24.21	MYC, THEM75	LINC00 824	Ovarian cancer	Goode EL. A genome-wide association study identifies susceptibility loci for ovarian cancer at 2q31 and 8q24. Nat Genet. 2010 Oct;42(10):874-9.
17q12	NR	HNF1B	High-grade serous ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
13q13.1	FRY	FRY	Cancer (pleiotropy)	Fehring G. Cross-Cancer Genome-Wide Analysis of Lung, Ovary, Breast, Prostate, and Colorectal Cancer Reveals Novel Pleiotropic Associations. Cancer Res. 2016 Sep 1;76(17):5103-14.

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Region	Reported Gene	Mapped Gene	Disease/Trait	Source
5p15.33	NR	TERT	Serous borderline ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
22q12.1	NR	TTC28, LOC101929594	Serous invasive ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
17q21.32	NR	SKAP1	Ovarian cancer	Pharoah PD. GWAS meta-analysis and replication identifies three new susceptibility loci for ovarian cancer. Nat Genet. 2013 Apr;45(4):362-70, 370e1-2.
8q21.13	CHMP4C, FABP5, PMP2, FABP12, IMPA1, SLC10A5, ZFAND1, SNX16, FABP4	CHMP4C	Ovarian cancer	Pharoah PD. GWAS meta-analysis and replication identifies three new susceptibility loci for ovarian cancer. Nat Genet. 2013 Apr;45(4):362-70, 370e1-2.
17q12	NR	HNF1B	Ovarian clear cell cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
10p12.31	NR	MLLT10	Serous invasive ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
17q12	NR	HNF1B	Epithelial ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
17q21.31	intergenic	PLEKH M1	Ovarian cancer in BRCA1 mutation carriers	Couch FJ. Genome-wide association study in BRCA1 mutation carriers identifies novel loci associated with breast and ovarian cancer risk. PLoS Genet. 2013;9(3):e1003212.
17q21.31	NR	PLEKH M1	Ovarian cancer in BRCA1 mutation carriers	Couch FJ. Genome-wide association study in BRCA1 mutation carriers identifies novel loci associated with breast and ovarian cancer risk. PLoS Genet. 2013;9(3):e1003212.

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Region	Reported Gene	Mapped Gene	Disease/Trait	Source
17q12	NR	HNF1B	Serous invasive ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.
22q12.1	NR	TTC28, LOC101929594	High-grade serous ovarian cancer	Phelan CM. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. 2017 May;49(5):680-691.

* In some instances, no region or mapped gene is identified for a given SNP. Most likely, these are in regulatory regions that undergo looping to the gene of interest, but the looping has not been defined yet.

APPENDIX B

22 February 2019

CURRICULUM VITAE

Name: Benjamin G. Neel

Office Address: Laura and Isaac Perlmutter Cancer Center
522 First Avenue
Smilow Building 12th Floor, Suite 1201
New York, NY 10016
Tel: 212.263.3019, Fax: 212.263.9190
benjamin.neel@nyulangone.org

Education:

05/1977 A.B. Cornell University College of Arts and Sciences, Ithaca, NY
06/1982 Ph.D. Rockefeller University, New York, NY
06/1983 M.D. Cornell University Medical College, New York, NY

Postdoctoral Training:

Internship and Residencies:

1983-1985 Medical Resident, Beth Israel Hospital, Boston, MA
1985-1987 Special Resident, Beth Israel Hospital, Boston, MA

Research Fellowships:

1985-1989 Special Fellow, Leukemia Society of America (Molecular Biology), Harvard University Department of Cell and Developmental Biology, Cambridge, MA
1987-1988 Postdoctoral Fellow, Harvard University Department of Cell and Developmental Biology, Cambridge, MA

Academic Appointment:

1988-1993 Assistant Professor of Medicine, Harvard Medical School, Boston, MA
1993-1999 Associate Professor of Medicine, Harvard Medical School, Boston, MA
1999-2007 Professor of Medicine, Harvard Medical School, Boston, MA
2006 -2007 William B. Castle Professor of Medicine, Harvard Medical School, Boston, MA
2007 -2015 Professor of Medical Biophysics, University of Toronto, Toronto, ON
2007 - 2015 Canada Research Chair, Tier 1
2015- Professor of Medicine, NYU Langone Health, School of Medicine, New York, NY

Hospital Appointment:

1994-2007 Director, Cancer Biology Program, Beth Israel Deaconess Medical Center
2003-2007 Deputy Director, Basic Research, Hematology/Oncology Division, Beth Israel Deaconess Medical Center, Boston, MA
2007- 2014 Director, Research, Princess Margaret Hospital Cancer Center, Toronto, ON
2008- 2014 Founding Director, The Campbell Family Institute for Cancer Research
2015- Laura and Isaac Perlmutter Cancer Center Director, NYU Langone Health, School of Medicine, New York, NY

Others:

2015- SiriusXM, Co-Host, Doctor Radio Oncology Special

Licensure and Certification:

1987 Diplomat, American Board of Internal Medicine
1984 Massachusetts License (inactive)

Awards and Honors:

1976 Phi Beta Kappa
1977 Phi Kappa Phi
1983 Associated Medical Schools of New York, Award for Biomedical Research
1985 Special Fellowship, Leukemia Society of America
1990 Harvard University Nominee for Pew Scholars Program
1992 Harvard University/Hoffman-LaRoche Institute for Chemistry and Medicine
Grant Recipient
1992 American Cancer Society, Junior Faculty Research Award
1992 American Association for Cancer Research, Gertrude Elion Award
2003, 2008 NIH MERIT Award (Renewed)
2007- Canada Research Chair, Tier 1
2009- Premier of Ontario Summit Award
2012- 2015 AACR Board of Directors, Elected
2015- Association of American Physicians, Elected Member

Selected Invited Talks:

1996 EMBO Workshop on Protein Dephosphorylation, Switzerland
1996 British Society of Cell Biology Joint Spring Meeting, U.K.
1996 Hanson Symposium on Molecular Mechanisms of Oncogenesis,
Adelaide, Australia
1997 Keystone Meeting on Cell Signaling, Colorado
1997 FASEB Summer Research Conference on Hematopoietic
Neoplasms, Vermont
1997 EMBO-FEBS Workshop on Protein Phosphatases and Protein
Dephosphorylation, Oxford, England
1997 Tokyo International Symposium, Tokyo, Japan
1998 Keystone Meeting on JAK/STAT Signalling, Colorado
1998 Gordon Research Conference on Second Messengers and
Protein Phosphorylation, New Hampshire
1998 FASEB Summer Research Conference on Protein Phosphatases,
Copper Mountain, Colorado
1998 International Hematology Congress, Amsterdam
1998 University of Toronto Department of Immunology Eaton Lectureship
1999 First Harvard/Munich AML Workshop, Munich, Germany
1999 FASEB Meeting on Biology of ImmunoReceptors, Saxtons River, Vermont
2000 Lorne Cancer Conference, Lorne, Australia
2000 FASEB Meeting on Signal Transduction in the Immune System, Saxtons
River, Vermont
2000 The Second International Conference on Signal Transduction, Dubrovnik,
Croatia
2001 FASEB Meeting on Receptors and Signal Transduction, Cooper Mountain,
Colorado
2001 American Heart Association Annual Meeting, Washington, DC
2002 Experimental Biology 2002, New Orleans, Louisiana

2002 Keystone Symposium on Molecular and Cellular Biology of Leukocyte Receptors, Lake Tahoe, California

2002 Fifth International Conference on Phosphatases and Cellular Regulation, Okazaki, Japan

2003 Europhosphatases 2003, Barcelona, Spain

2003 Gordon Conference on Cell Proliferation, New London, New Hampshire

2003 FASEB Summer Research Conference on Signal Transduction in the Immune System, Snowmass Village, Colorado

2004 12th International Conference on Second Messengers and Phosphoproteins, Montreal, Quebec, Canada

2004 FASEB Summer Research Conference on Protein Phosphatases, Snowmass Village, Colorado

2005 AACR Annual Meeting, Anaheim, California, Meet the Experts

2005 Keynote Speaker, National Neurofibromatosis International Consortium for the Molecular Biology of NF1 and NF2, Aspen, Colorado

2005 17th Pezcoller Symposium on Molecular Understanding of Solid Tumors, Trento, Italy

2005 Europhosphatases 2005, Cambridge, England

2005 FASEB Summer Research Conference on Hematological Malignancies, Saxton's River, Vermont

2005 FASEB Summer Research Conference on Growth Factor Receptor Tyrosine Kinases in Mitogenesis, Morphogenesis and Tumorigenesis Tucson, Arizona

2005 Salk/EMBL Oncogenes and Growth Control Meeting, La Jolla, California

2006 International Symposium of Kobe University on Signal Transduction, Kobe, Japan

2007 USA-Japan Cooperative Cancer Workshop on Animal Models of Hematological Malignancies, Kauai, Hawaii

2007 5th International Aachen Symposium on Cytokine Signaling, Aachen, Germany

2007 AACR Annual Meeting, Los Angeles, California, Meet the Expert

2007 Signaling and Metabolic Pathways in Cancer Workshop, Madrid, Spain

2007 FASEB Summer Research Conference on Growth Factor Receptor Tyrosine Kinases in Mitogenesis, Morphogenesis and Tumorigenesis, Tucson, Arizona

2008 20th Lorne Cancer Conference, Lorne, Australia

2008 FASEB Summer Research Conference on Protein Phosphatase Snowmass Village, Colorado

2008 Gordon Research Conference on Growth Factors and Signalling, Oxford, United Kingdom

2011 AACR Annual Meeting, Forum on Cancer Stem Cells, Moderator and Speaker

2011 Avery Steelman Lecture, University of North Carolina, Department of Pharmacology.

2012 Satellite Conference on Protein Phosphatases, Melbourne, Australia

2012 Lorne Proteomics Conference, Lorne, Australia

2012 Lorne Cancer Conference, Lorne, Australia

2012 Pathways Symposium, Koch Institute, MIT, Cambridge, MA

2012 Keynote speaker 2013 Japanese Phosphatase Meeting, Tokyo Japan

2013 Invited Speaker, AACR Conference on Synthetic Lethality, Seattle, WA

2013	Arnold S. Greenberg Lecture, U. Winnepeg
2014	Invited Speaker, Europhosphatase Meeting, Rehovot, Israel
2013	Keynote Speaker, International Conference on Systems Biology, Copenhagen, Denmark
2014	Session Chair and Invited Speaker, Current Topics in Ovarian Cancer, AACR Annual Meeting, San Diego, CA.
2014	Christie Gordon Lecture, University of Birmingham, Birmingham UK
2014	Invited Speaker, FASEB phosphatases Meeting, Nassau, Bahamas
2014	Invited Speaker, Salk Meeting on Cell Signaling, La Jolla, CA
2014	Invited Speaker, Max Planck Institute Student Symposium, Dortmund, Germany
2014	Invited Speaker, Japanese Phosphatase Society Meeting
2015	Keystone Speaker, the Biological Code of Cell Signaling - A Tribute to Tony Pawson, Steamboat Springs, Colorado
2015	Invited Speaker, Department of Oncological Sciences at Mount Sinai, New York, New York
2015	Invited Speaker, Current Topics in Cancer Therapy, AACR Annual Meeting, Philadelphia, PA
2015	Invited Speaker, Cell Signalling and its Therapeutic Implications (CSTI) Symposium, Melbourne, Australia
2015	Invited Speaker, Monash University, Melbourne, Australia
2015	Invited Speaker, Uppsala University, Uppsala, Sweden
2015	Invited Speaker, EMBO Conference Europhosphatase Meeting, Turku, Finland
2015	Invited Speaker, FASEB Protein Kinases and Protein Phosphorylation Meeting, Itasca, Illinois
2015	Oncology Grand Rounds Speaker, Georgetown-Lombardi Comprehensive Cancer Center, Washington, District of Columbia
2016	Pharmacology Seminar Course Speaker, Precision Medicine and Pharmacology at UCSD University of California, San Diego, La Jolla, California
2016	Regulatory Networks in Health and Disease Seminar Series Speaker, Department of Pharmacology and Cancer Biology at Duke Cancer Institute at Duke University School of Medicine, Durham, North Carolina
2016	Invited Speaker, 213 th Interurban Clinical Club, New York, New York
2016	Invited Speaker, Hinterzartner Kreis on Cancer Research, Lake Como, Italy
2016	Guest Speaker, 81st Cold Spring Harbor Laboratory Symposium on Quantitative Biology, Cold Spring Harbor, NY
2016	Invited Speaker, FASEB Science Research Conference on Cell Signaling in Cancer: From Mechanisms to Therapy, Snowmass, Colorado
2016	Invited Speaker, Lurie Comprehensive Cancer Center of Northwestern University, Hematology/Oncology, Grand Rounds, Chicago, Illinois
2016	Invited Speaker, Biochemical Society meeting on Phosphatases and Signalling in Health and Disease, University of Bath, Claverton Down, Bath
2016	Invited Speaker, FASEB Science Research Conference on Protein Phosphatases, Steamboat Springs, Colorado
2016	Invited Speaker, Post-Translational Regulation of Cell Signaling Meeting, Salk Institute, La Jolla, California
2016	Invited Speaker, Oncology Seminar Series, Lilly NY Research, New York, New York

- 2016 Invited Speaker, Animal models for hematopoietic malignancies, Nice, France
- 2016 Guest Speaker, 12th International Conference on Protein Phosphates, Kinki University, Osaka, Japan
- 2016 Seminar Speaker, Cold Spring Harbor Laboratory Seminar Series, Cold Spring Harbor, NY
- 2016 Visiting Lecturer, Frontiers in Oncology Lecture, Icahn School of Medicine at Mount Sinai Hospital, New York, New York
- 2016 Invited Speaker, Tisch Cancer Institute Grand Rounds Lecture, Icahn School of Medicine at Mount Sinai Hospital, New York, NY
- 2017 Dana-Farber Cancer Institute, Louise & Herbert Shivek, Oncology Lecture Series, Boston, MA
- 2017 UCSF Helen Diller Family Comprehensive Cancer Center, Seminar Series, San Francisco, CA
- 2017 Invited Speaker, University of Turku, Frontiers of Science Seminars, Turku, Finland
- 2017 Invited Speaker, Charite University Medical Center, Sharing Radically Novel Visions in Cancer Conference, Berlin Germany
- 2017 Invited Speaker, Meyer Cancer Center at Weill Cornell Medicine, Seminar Series, New York, NY
- 2017 Invited Speaker, EMBO Europhosphatase, Paris, France
- 2017 Invited Speaker, FASEB - Protein Kinases and Protein Phosphorylation, Cambridge, UK.
- 2017 Invited Speaker, New York Genome Center, New York, NY
- 2017 Invited Speaker, Cold Spring Harbor Asia Conference on Cell Signaling & Metabolism in Metabolism in Development & Disease, Suzhou, China.
- 2018 Invited Speaker, World Congress on Cancer, Jaipur, India.
- 2018 Invited Speaker, University of Texas MD Anderson Cancer Center, Blaffer Lecture Series, Houston, TX.
- 2018 Invited Speaker, European Association for Cancer Research, LIF AS WE KNOW IT Conference, Barcelona, Spain.
- 2018 Invited Speaker, FASEB -Cell Signaling in Cancer: from Mechanisms to Therapy, Steamboat Springs, Colorado
- 2018 Distinguished Lectureship, Albert Einstein Cancer Center, New York, NY.
- 2018 Invited Speaker, Salk Post-translational Regulation of Cell Signaling, La Jolla, CA.
- 2018 Distinguished Lectureship, University of Cincinnati College of Medicine, Cincinnati, OH.
- 2018 Invite Speaker, International Phosphatase Conference, Tokyo, Japan
- 2018 Invited Speaker, Science China Life Science Conferences on Cell Signaling, Hangzhou and Wuhan, China
- 2018 Invited Speaker, Rhode Island Hospital's Department of Hematology and Oncology Research, Scientific Meeting.

Meetings Organized:

1995, 1997 Co-Organizer, Cold Spring Harbor Laboratory Meeting on Tyrosine
 1999, 2001 Phosphorylation and Cell Signaling, New York
 2003, 2005
 2007, 2009
 1999 Vice-Chair (elected), Gordon Conference on Cell Proliferation
 2000 Vice-Chair (elected), FASEB Phosphatase Meeting
 2001 Chair (elected), Gordon Conference on Cell Proliferation
 2002 Chair (elected), FASEB Phosphatase Meeting
 2011 Chair, 2012 AACR Annual Meeting Program Committee
 2014 Co-organizer, Cold Spring Harbor Laboratory Meeting on Mechanisms and
 Models of Cancer
 2015 Co-Chair, AACR Ovarian Cancer Conference, Orlando, Florida
 2015 Co-Chair, WIN Symposium 2016, Paris, France

Editorial Boards:

1993- Editorial Board Member, Virology
 1995-2000 Editorial Board Member, Journal of Biological Chemistry
 1997- Editorial Board Member, Cell Growth and Differentiation
 1997-2000 Editorial Board Member, Genes and Development
 1996-2000 Editorial Board Member, Molecular and Cellular Biology
 2000-2010 Editor, Molecular and Cellular Biology
 2002- Editorial Board Member, Cancer Cell
 2009- Editorial Board Member, Current Opinion in Genetics and Development
 2010- Editorial Board Member, Journal of Experimental Medicine
 2010- 2014 Board of Reviewing Editors, Science Signaling
 2011- Editorial Board Member, AACR, Cancer Discovery
 2013- Editorial Board Member, Journal of Clinical Investigation
 2014- Editorial Board Member, Molecular Cell

Board Members:

2015- 2016 Centre for Commercialization of Antibodies and Biologics (CCAB), Board and
 Chair
 2010-2016 Kolltan, Scientific Advisory Board
 2014-2018 Northern Biologics, Member, Board of Directors
 2014- Northern Biologics, Co-founder and Scientific Advisory Board
 2014- Gerstner School, Memorial Sloan Kettering, External Advisory Committee
 2015- Ronald McDonald House of New York, Board of Directors
 2016- Lurie Comprehensive Cancer Center of Northwestern University, External
 Advisor Board
 2016- AACR Regional Advisory Subcommittee on Canada
 2017- Rutgers Cancer Institute of New Jersey, External Advisory Board
 2017- Co-Founder and Chair, Scientific Advisory Board, Navire Pharmaceuticals
 2017- Quantigic Genomics LLC, Scientific Advisory Board
 2017- Herbert Irving Comprehensive Cancer Center, at Columbia University Medical,
 External Scientific Advisory Board
 2018- AACI Board of Directors

2018- Max F. Perutz Laboratories, Scientific Advisory Board

Memberships and Professional Societies:

American Society for Microbiology (ASM)
American Association for Cancer Research (AACR)
American Association of Arts and Sciences (AAAS)
American Society of Hematology (ASH)
Affiliate Member of the New York Genome Center

Study Sections:

1992 Ad Hoc Reviewer for NIH DSR IRG Study Section
1993, 1994 Study Section member, California State Tobacco Related Diseases Program
1995 Ad Hoc Reviewer, Veterans Administration
1995 Ad Hoc Reviewer, Israeli National Science Foundation
1996 Reviewer for NCI-Frederick Intramural Program
1995-1998 Member, NIH Biology II Study Section
1997-2001 Study Section member, American Cancer Society, Mass. Division
1998-2000 Member, NIH Molecular Biology Study Section (CDF-1)
1997-2007 Study Section member, The Medical Foundation, Boston, MA
2004 Member, Hematology Study Section
2004 Reviewer, California State Breast Cancer Research Program
2007-2010 Reviewer, STARR Cancer Consortium
2008-2011 Study Section Member, Molecular and Integrative Signal Transduction (MIST)
2010-2015 Member, Gairdner Award Medical Advisory Board (Selection Committee)
2016 Ad Hoc Reviewer, Winship Cancer Center of Emory University
2016 Reviewer, Howard Hughes Medical Institute, Investigator Review
2016-2018 Member, AACR Award for Lifetime Achievement in Cancer Research
Selection Committee
2018 Chairperson, AACR Award for Lifetime Achievement in Cancer Research
Selection Committee

Major Research Interests:

Tyrosine phosphatases, scaffolding adapters, signal transduction, mouse models of signaling abnormalities and human disease, breast carcinogenesis, leukemogenesis, functional genomic screening, ovarian cancer.

Teaching Experience:

1990-1993 Co-director, Cellular and Developmental Biology 200B: core cell biology course in Cell Biology, Division of Medical Sciences, Harvard University
1993 Lecturer, Immunology 212 and Genetics 205
1994 Lecturer, Core Cell Biology Course (CDB200B)
1995-2006 Section Leader, Core Cell Biology Course (CDB200B)
2004-2006 Co-Director, Cell Biology and Biochemistry core course, Harvard Medical School
2004-2006 Co-Director, CB201 (Core graduate student Cell Biology Course)
2013-2014 Lecturer, Signaling in Biochemistry - (BCH426) - Phosphatases
2013-2014 Lecturer, Medical Biophysics Lecture – (MBP1007) - RTK signaling

Patents:

Methods for identifying a tyrosine phosphatase abnormality associated with neoplastic disease.

Inventors: Freeman, Jr.; Robert M. (Boston, MA); Plutzky; Jorge (Boston, MA); Neel; Benjamin G. (Wayland, MA); Rosenberg; Robert D. (Brookline, MA) 5,536,636 - July 16th, 1996

Peptide which binds SH.sub.2 domains of protein tyrosine phosphatase SH-PTP1.

Inventors: Klingmuller; Ursula (Arlington, MA); Michnick; Stephen (Westmount, CA); Neel; Benjamin G. (Wayland, MA); Lorenz; Ulrike (Boston, MA); Lodish; Harvey F. (Brookline, MA) 5,659,012 - August 9th, 1997

Activated mutants of SH2-domain-containing protein tyrosine phosphatases and methods of use thereof.

Inventors: Neel, Benjamin G (Wayland, MA).; O'Reilly, Alana M. (Watertown, MA); Shoelson, Steven (Natick, MA); Pluskey, Scott (Allston, MA) 6,156,551 - Dec. 5th, 2000

Gab2(p97) gene and methods of use thereof .

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Inventors: Neel, Benjamin G. and Mohi, Golam. US 2006/0094674 A1 – May 4th, 2006

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Inventors: Neel, Benjamin G, Roberts, Amy, Kucherlapati, Raju, Araki, Toshiyuki, Swanson, KD. US 2010/0227778 A1 - September 9th, 2010

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APPENDIX C

Previous Four Years of Expert Testimony for Benjamin Neel, M.D., Ph.D.

Dr. Benjamin Neel has not testified as an expert at trial or by deposition during the previous four years.

Exhibit F

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY**

**IN RE: JOHNSON & JOHNSON TALCUM
POWDER PRODUCTS MARKETING, SALES
PRACTICES AND PRODUCTS LIABILITY
LITIGATION**

MDL NO. 16-2738 (FLW) (LHG)

THIS DOCUMENT RELATES TO ALL CASES

**EXPERT REPORT OF IE-MING SHIH, MD, PHD
FOR GENERAL CAUSATION *DAUBERT* HEARING**

Date: February 25, 2019

A handwritten signature in black ink, appearing to read "Ie-Ming Shih", written above a horizontal line.

Ie-Ming Shih, MD, PhD

EXPERT REPORT ON THE ALLEGED CAUSAL ROLE OF TALC IN OVARIAN CANCER

Ie-Ming Shih, MD, PhD

Richard W. TeLinde Distinguished Professor of Gynecologic Pathology
Director of the inter-departmental TeLinde Gynecologic Pathology Research Program
Co-Director of the Breast and Ovarian Cancer program, Sidney Kimmel Comprehensive Cancer
Center
Johns Hopkins University School of Medicine
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INTRODUCTION, SCOPE OF REPORT, AND SUMMARY OF OPINIONS

I understand that plaintiffs' experts – in particular, Dr. Ghassan Saed and Dr. Sarah Kane – have offered opinions for litigation regarding the biological mechanisms by which perineal talc might cause or worsen the prognosis of ovarian cancer. I was asked to review these litigation opinions and to assess their scientific validity and the reliability of the methods employed to formulate them. Based on my experience and expertise as a pathologist who focuses on gynecological pathology and carcinogenesis, I have formed the following opinions, which I detail in this report:

1. Dr. Saed's and Dr. Kane's opinions related to the biological plausibility of the theory that talc powder use can cause ovarian cancer or increase the risk of ovarian cancer are not the product of reliable methods and are contrary to established scientific knowledge.
2. Dr. Saed's experimental results, including those published (in press), are fraught with research design flaws, and the results fail to support or negate his hypothesis – they are simply irrelevant. He has not developed any evidence that supports the theory that talc powder has a carcinogenic role in ovarian cancer development.
3. Based on the recent research findings as published, I did not find any evidence – molecular, biological, pathological or epidemiological in nature – that supports the conclusion that talc can cause or increase the risk of ovarian cancer.
4. Dr. Saed failed to provide an adequate disclosure of a significant conflict of interest in his manuscript, and his failure to do so calls all of his work and conclusions into question.

SUMMARY OF RELEVANT EXPERIENCE AND QUALIFICATIONS

I am a pathologist with expertise in gynecologic pathology, especially in the carcinogenesis and etiology of ovarian cancer (i.e., how ovarian cancer develops in women). I am certified in Anatomic Pathology by the American Board of Pathology. I received my medical degree from the Taipei Medical University in 1988, as well as a Ph.D. in Biomedical Graduate Study (Pathology) from the University of Pennsylvania in 1993. Thereafter, I completed a residency in Anatomic Pathology and a clinical fellowship in Gynecologic Pathology at the Johns Hopkins Hospital, and a research fellowship in Cancer Genetics at Johns Hopkins Oncology Center.

I currently hold an appointment as the Richard W. TeLinde Distinguished Professor of Gynecologic Pathology in the Department of Gynecology and Obstetrics at Johns Hopkins Medical Institutions (see the link below), where I also hold secondary appointments in the Departments of Oncology and Pathology. I additionally serve as the Director of the Johns Hopkins Inter-departmental TeLinde Gynecologic Pathology Research Program (www.gynecologycancer.org) and as a Co-director of the Breast and Ovarian Cancer Program at the Sidney Kimmel Comprehensive Cancer Center at the Johns Hopkins University School of Medicine. Of note, the Richard W. TeLinde distinguished (endowed) professorship is considered the most prestigious position of gynecologic pathology in the country. <https://professorships.jhu.edu/professorship/richard-w-telinde-distinguished-professorship-in-gynecological-pathology/>.

My research focuses on exploring carcinogenesis, genomic landscapes and pathogenesis of ovarian and endometrial cancers, developing new target-based therapy and applying innovative technology for early detection of gynecologic cancer. My research team has proposed the new model in classifying ovarian cancer, which has become widely used, helped elucidate the origin of ovarian cancer and develops new technology to detect ovarian cancer. My research group also pioneered elucidating the molecular landscapes in different types of ovarian cancer and identifying novel genes and pathways involved in cancer initiation, chromatin remodeling, chromosomal instability, cytokinesis and tumor invasion in ovarian cancer, providing new insight into how ovarian cancer occurs.

I have received many research awards from US government agencies, including the National Institutes of Health (“NIH”) and National Cancer Institute (“NCI”) and the Department of Defense (DoD), to study ovarian cancer-related topics. Pursuant to these awards, my research team, in collaboration with medical and gynecologic oncologists, is initiating new clinical trials that capitalize on our new molecular research findings. For example, I am the Principal Investigator in the recent NIH/NCI awarded SPORE (Specialized Program of Research Excellence) for Ovarian Cancer (\$12.5 million for 5 years, 2018-2023), and I am leading the multi-institutional team for translational ovarian cancer research, including the development of early detection and novel therapies by further understanding ovarian cancer initiation and progression and by better understanding ovarian cancer biology. I have also been the Principal Investigator or key project leader in several research projects supported by NIH/NCI, DoD and several private foundation awards. Under my leadership, the TeLinde Gynecologic Pathology Research Program has generated more than \$6.6 million of research funds each year, making my research program the most successful gynecologic pathology research group in the country.

I have published more than 350 original articles and book chapters in prestigious medical and science journals such as *New England Journal of Medicine*, *Cancer Cell*, *Journal of National Cancer Institute*, *PNAS*, *Science*, *Lancet Oncology*, *Nature* and *Nature Medicine*, etc., which have been cited more than 32,000 times in the literature, making me one of the most cited gynecologic pathologists in the world. My 2017 paper published in *New England Journal of Medicine* (related to molecular changes in the very beginning of a specific type of ovarian cancer) received the Most Influential Paper Prize in Gynecology field in 2017 from the Columbia Hospital for Women Research Foundation. I am also one of the contributors to book chapters in gynecology textbooks and the WHO Classification of Tumors of Female Reproductive Organs

published by the IARC 2014 in defining different types of ovarian cancer. I have been invited to give more than 110 lectures worldwide, many of which related to ovarian cancer. In particular, I have given 36 invited lectures on the carcinogenesis of ovarian (high-grade) cancer. These lectures reflect my academic status and international reputation on the subject of how ovarian cancer develops. I have been on several advisory boards, such as the NCI Ovarian Task Force of Gynecologic Cancer Steering Committee and Ovarian Cancer Research Alliance, and served as an editorial board member of *Cancer Research*, *Journal of Pathology*, *American Journal of Pathology* and several others.

I am serving as an expert on ovarian cancer carcinogenesis in this litigation. In particular, I was asked to review the expert report and related work of Dr. Ghassan Saed. My reimbursement rate is commensurate to my experience and academic status mentioned above: \$800/hr for preparing reports, \$1400/hr for deposition, \$1200/case for reviewing tissue materials and generating pathology reports.

OPINIONS

The following opinions are based on my expertise, experience, training, my previous and ongoing research, as well as knowledge from reading the relevant scientific literature. Based on an assessment of the totality of the evidence, and following the methodology set forth below, I hold the opinions offered in this report to a reasonable degree of scientific and medical certainty. I reserve the right to amend or supplement this report as new information becomes available.

This report is divided into four sections. I begin with a brief overview (section A). I then express my opinions in two parts. Section B sets forth the serious problems with Dr. Saed's research findings provided in his expert report and the in-press article. I conclude that Dr. Saed's research does not support the conclusions he offers in his expert report or his article. Section C addresses my understanding of whether talc powder is a cause of ovarian cancer, including the lack of scientific evidence to support the conclusion that talc could cause ovarian cancer. And Section D discusses the problematic implications of Dr. Saed's failure to disclose in his manuscript that the funding he received was from a law firm with a vested interest in the results of his study.

A. Overview

Very few true ovarian cancer risks have been established. They include the BRCA1/2 inherited mutations and the increased accumulated times of ovulation in a woman's lifetime (affected by oral contraceptive use, oocyte induction, child bearing, breast feeding, etc.). Approximately 1.3% of women in the general population will develop ovarian cancer sometime during their lives (Howlader et al., 2017). But in women who carry the germline mutations, the chance dramatically increases by the age of 80 to ~ 44% of women who inherit a harmful BRCA1 mutation and ~ 17% of women who inherit a harmful BRCA2 mutation (Kuchenbaecker et al., 2017). Ovarian cancer precursor lesions are also enriched in BRCA1/2 mutation carriers (Visvanathan et al., 2018). Similarly, more ovulations increase the risk of ovarian cancer, the so-called "incessant ovulation theory" of ovarian cancer (Fathalla, 2013; Havrilesky et al., 2013; Lurie et al., 2008). The above conclusions are reproducible and unequivocal and have become generally accepted in the field of ovarian cancer carcinogenesis.

Several studies have reported an association between ovarian cancer and the use of talcum powder on the perineal area. In 2010, the International Agency for Research on Cancer (“IARC”) classified perineal use of talc as a possible carcinogen. As compared to the published reports confirming scientifically accepted ovarian cancer risks, the studies focusing on delineating the alleged ovarian cancer-promoting roles of talc are fraught with several issues, including study design, incorrect interpretation of the study results, and premature conclusions. Therefore, credible support for the theory that talc can cause ovarian cancer is lacking. In Section C of this report, I will carefully examine the published evidence (especially after 2010) that is related to the alleged role of talc in the development of ovarian cancer.

B. Dr. Saed’s And Dr. Kane’s Conclusions

In this part, I identify problems related to the interpretations and conclusions made by Dr. Saed, who conducted experiments on talc powder and argues that talc could cause ovarian cancer development, as well as the opinions of Dr. Kane, who puts forth a number of the same points raised by Dr. Saed but also offers a few additional opinions of her own. I first address Dr. Saed’s opinions (B.1) and in-press article (B.2). I then address the additional opinions offered by Dr. Kane (B.3).

1. Dr. Saed’s statements in his expert report

Dr. Saed purports to have conducted laboratory research that supports the theory that talc use can cause ovarian cancer. According to Dr. Saed:

“1. Johnson’s Baby Powder elicits an inflammatory response in normal ovarian and tubal cells and in ovarian cancer cells that can result in the development and progression of ovarian cancer.” (See, e.g., Saed Rep. at 20; see also id. at 10.)

“2. This pro-carcinogenic process involves oxidative stress, alteration of the redox environment by increasing oxidant enzymes and decreasing anti-oxidant enzymes, promotion of cell proliferation, inhibition of apoptosis, and induction of specific genetic mutations.” (See, e.g., Saed Rep. at 20; see also id. at 16-17.)

“3. Johnson’s Baby Powder exposure results in elevation of CA-125, a clinically relevant biomarker for ovarian cancer, in normal and ovarian cancer cells.” (See, e.g., Saed Rep. at 20; see also id. at 18.)

“4. The molecular effects resulting from Johnson’s Baby Powder exposure exhibit a clear dose-response pattern.” (See, e.g., Saed Rep. at 20; see also id. at 17.)

Dr. Saed concludes that “Johnson’s Baby Powder exposure can cause ovarian cancer.” (See, e.g., Saed Rep. at 20.)

Dr. Saed’s research is unreliable and his conclusions reveal a fundamental misunderstanding of ovarian cancer, for several reasons.

Excessive Talc Concentration. The talc concentrations used in Dr. Saed’s experiments (from 20-100 mg/ml) are higher than would be encountered in real-world (i.e., physiological) conditions. If use of such a high concentration was deemed appropriate by the researcher, he

needed to show a similar talc concentration range in human gynecologic tissues from those who had prior exposures. Otherwise, his data cannot be extrapolated to patients in real life. But no such showing was made here. Therefore, the observations made in Dr. Saed's report concerning cell growth, inhibition of cell death (apoptosis) and CAT expression and enzymatic activity in epithelial ovarian cancer cell lines and other cell lines (which are not relevant to ovarian cancer initiation) – are most likely the results of abnormally high concentrations of talc, which is not relevant to human biology.

Use of Cancer Cell Lines. Dr. Saed's study is also problematic because, although he was attempting to support the hypothesis that talc powder can cause ovarian cancer, Dr. Saed's study relies extensively on claimed effects of talc powder (under a non-physiological concentration) on cancer cell lines. Cancer cell lines were originally derived from cancer tissues and they are already cancer cells, meaning not normal cells anymore. If one wishes to show that the chemical of interest is potentially carcinogenic, one should show its biological effects on normal non-transformed cells – in this case, the normal fallopian tube epithelial cells. But this was not reported in Dr. Saed's study. (Dr. Saed did include immortalized cancer-free cells as well, but these are not normal cells.) Therefore, the research team missed the point regarding whether talc particles can cause ovarian cancer. Another problem with the study design is that the researchers mistakenly used an A2780 cell line as an ovarian high-grade serous cancer cell line. But in fact, A2780 is unlikely an ovarian high-grade serous cancer line and should not have been relevant in this study, reflecting the limited knowledge of the research group in studying ovarian cancer (Anglesio et al., 2013; Domcke et al., 2013).

Another related concern is the experiment related to oxidative stress. According to Dr. Saed, there is “*substantial evidence demonstrating that altered oxidative stress may play a role in maintaining the oncogenic phenotype of [epithelial ovarian cancer] cells.*” (See, e.g., Saed Rep. at 17-18 (emphasis added).) But again, Dr. Saed's research does not show whether this is true in normal fallopian tube epithelial cells that give rise to ovarian cancer. In fact, what Dr. Saed really showed is the effect on cancer cells, which are characterized by a very different molecular and biological landscape from normal counterparts. If one wishes to demonstrate whether the chemical can induce malignant changes, one should focus on studying the effects of the chemical on normal fallopian tube epithelial cells.

Irrelevance of CA-125 Finding. Dr. Saed misstates the relevance of his findings with respect to CA-125. CA-125 is an FDA-approved ovarian cancer biomarker for monitoring disease status after treatment. It is definitely not a cancer-specific biomarker, as many normal tissues express CA-125 in the absence of cancer or its precursor. Therefore, CA-125 should not be considered as indicating the onset or heightened risk of the development of ovarian cancer. Thus, Dr. Saed's statement in the conclusion of his report that CA-125 is a “clinically relevant biomarker for ovarian cancer” (see, e.g., Saed Rep. at 20) is misleading, and the data from CA-125 are not relevant to support the researcher's conclusion.

Extrapolation From In Vivo Experiment. Dr. Saed claims in his summary paragraph that “*This study has shown a dose-dependent significant increase in key pro-oxidants . . . and a concomitant decrease in key antioxidant enzymes . . . in all talc treated cells (both normal and ovarian cancer) compared to their controls.*” (See, e.g., Saed Rep. at 19.) But the significance of

this finding is unclear. Although a dose-dependent phenomenon is relevant to assessing causal effect in biological studies, a broader conclusion on causation would depend on demonstration of a similar dose-dependent effect in women – i.e., that women who apply talc perineally have a higher risk when they are exposed to a higher dosage of talc powder (more frequent use and/or longer period of time, for example). Dr. Saed’s experiment obviously does not answer this question. Moreover, all the data as presented in Dr. Saed’s report were based on *in vitro* (in petri dishes or test tubes) experiments, and their significance to *in vivo* (in real animal or human tissues) is essentially unknown. Therefore, Dr. Saed’s leap to a causal conclusion in his “Summary of Opinions” is not supported from the perspective of careful scientific investigation.

Studies Not Conducted. Dr. Saed acknowledged that there are other studies that he could have conducted – and even proposed conducting – but chose not to conduct due to claimed limitations on time and money. For example, he testified that animal experiments would be necessary to confirm that his *in vitro* experiments actually modeled chronic inflammation (Saed Dep. vol. 2, 542:16-25), but he did not conduct animal studies because he did not “have the time to do it and the money” (Saed Dep. vol. 1, 50:10-13). Dr. Saed similarly explained that he ultimately decided not to conduct other tests he had initially proposed, including one that he deemed essential to establishing a “cause and effect” relationship between talc exposure and ovarian cancer, because such testing would have taken more time and money. (Saed Dep. vol. 2, 498:6-17, 501:14-502:5, 503:10-505:20, 509:23-510:9, 513:9-14.) But science is a purely evidence-based and evidence-driven discipline, and limitations of money and time (or other matters mentioned in Dr. Saed’s deposition, including reagents and assays) cannot excuse a lack of scientific rigor.

2. Dr. Saed’s “In-Press” Paper in *Reproductive Science*

There are several problems with Dr. Saed’s article as well, most of which are similar to the problems I have already identified with respect to his expert report.

Cell Lines. Three “ovarian cancer” cell lines were used in Dr. Saed’s research. SKOV3 and A2780 in this new publication are not true ovarian high-grade serous cancer cells (Anglesio et al., 2013; Domcke et al., 2013). The third cell line employed, TOV112D, is a known ovarian endometrioid carcinoma cell line (Anglesio et al., 2013). This is concerning because none of the three “ovarian” cancer cell lines used were derived from high-grade serous carcinoma, which is the most common histological subtype of ovarian cancer and the disease focus of several of plaintiffs’ epidemiology experts in this litigation.

Concentration. The talcum powder in this study was dissolved in DMSO at a concentration of 500 mg in 10 ml. (Manuscript at 5.) It is certainly unknown whether this concentration is relevant to ovarian tissue exposure to perineal use of talcum powder in women. Therefore, the significance of the results – including the expression levels of antioxidant enzymes, SOD, CAT, GPX and GSR as well as pro-oxidants, INOS, NO₂⁻/NO₃⁻ and MPO in normal and ovarian cancer cells – is unclear.

Purported Mutations. The Saed paper states that, “[r]emarkably, talc exposure induced specific point mutations that are known to alter the activity in some of these key enzymes.” (Manuscript at 2.) The gene variants that were reported by Saed were not listed as cancer driver genes

(Tamborero, 2013), and therefore their biological significance in initiating human ovarian cancer is totally unknown. There is no evidence demonstrating these variants occur significantly in human ovarian cancer either. In addition, this statement has no solid support from the data provided (Table 2). Single nucleotide polymorphisms (SNPs) – a type of genetic variation – did occur in certain enzymes in some cell lines, but the reported mutant allele frequency (MAF) was low in general. This discrepancy is significant. A fundamental tenet of cancer genetics is that the mutations that drive tumor development, such as *TP53*, *KRAS* and many others, should be much higher (> 50% in cancer cell lines and > 10% in cancer tissues because of contamination from normal tumor stromal cells). As an example, *KRAS* mutation is an established cancer driver event, and it usually mutates in one of a pair of alleles (inherited from either mother or father) but not in the other, so the MAF is 50%. Thus, the reported findings suggest that mutations likely occur as a random event. In fact, the authors also said in the Result section that, “[i]ntriguingly, talc treatment reversed this SNP genotype to the normal genotype (Table 2).” (Manuscript at 8.) Based on my expertise in biology and cancer genetics, I can attest that this result of genotyping is of unknown significance and in any event is not related to the risk of talcum powder in promoting ovarian cancer. This is because these changes will not significantly affect any functions of the enzyme (meaning that the mutations do not have carcinogenic potential) unless the biochemistry can provide further evidence to support a different finding. In short, showing SNP changes does not prove or even suggest that an exposure is carcinogenic. The investigator would need to show a malignant or pre-cancerous change in tissue – and Dr. Saed has not done this.

CA-125. The authors state that talc treatment increased CA-125 levels in normal and ovarian cancer cells. (Manuscript at 8.) But for the reasons explained above, this is of no biological significance at all. CA-125 (also known as mucin 16) is a “biomarker” to monitor ovarian cancer during treatment. It has nothing to do with the disease biology (development of ovarian cancer). Nor, in any event, is CA-125 specific to ovarian cancer or, indeed, cancer generally. In gynecologic pathology, women who have several benign diseases (not cancers) have an increased CA-125 level in serum. Gynecologic tissues such as normal fallopian tube epithelium express CA-125. The best interpretation is that the increased CA-125 levels reflect a cell response to environmental stress (talc powder) – and not that this response has anything to do with ovarian cancer.

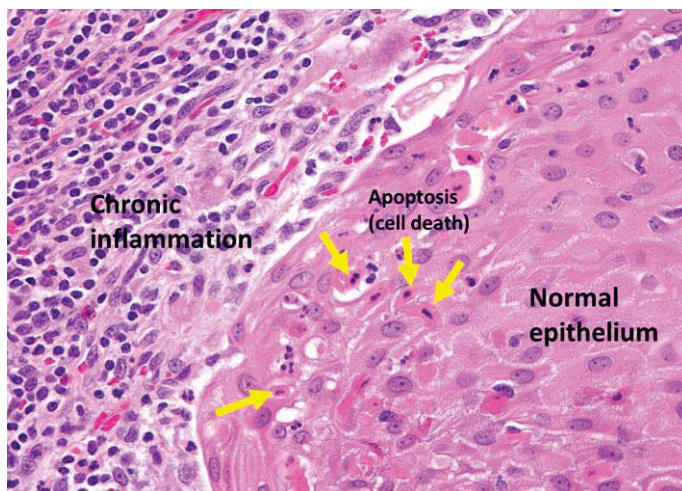


Figure 1. A representative photomicrograph showing the cell death (apoptosis) of epithelial cells in response to inflammation. There are many cells undergoing apoptosis (a kind of cell death) (arrows). These cells are characterized by pyknotic nuclei and eosinophilic condensed cytoplasm. Surrounding the epithelial nest are abundant lymphocytes and some leukocytes.

Cell Proliferation. The final conclusion provided in this paper is that the talc treatment increased cellular proliferation and decreased apoptosis (cell death). (Manuscript at 8.) But cell proliferation is not specific to cancer, as normal cells also proliferate all the time (like bone marrow blood cells and uterine epithelial cells) to replace normally aging cells. Thus, increased cellular proliferation itself does not suggest carcinogenicity. In other words, cellular proliferation is required but not sufficient to induce cancer. Rather, conceptually, if talc were a carcinogen, it would damage cell DNA first (mutagenic), causing either (1) growth arrest in non-transformed “normal” epithelial cells that repair DNA damage; or (2) cell death when the DNA damage is extensive and beyond the repair capacity of cells (**Figure 1**). But the result published is just the opposite (i.e., increased cell growth), and thus does not support the conclusion that talc is a mutagen or carcinogen. There are also numerous flaws associated with this experiment. For example, a time dependent cellular proliferation and apoptosis should be shown, different talc concentrations should be tested, more rigorous cell growth assays should be used, and more “normal” tubal epithelial and ovarian surface epithelial cells including the freshly prepared (non-transformed) ones should be used.

The assay for apoptosis suffered a similar pitfall in that other apoptotic markers should be employed. Moreover, reduced apoptosis itself is not a marker for tumorigenesis. In fact, apoptosis is more frequently seen in ovarian cancer precursor lesions and ovarian cancer than in normal counterparts (fallopian tube epithelium). And in any event, whether this talc-induced increased proliferation and decreased apoptosis can be observed *in vivo* is not known. Therefore, these *in vitro* results and conclusions cannot be extrapolated to support the hypothesis that talc use can cause ovarian cancer.

3. Dr. Kane’s Opinions

Dr. Kane has also expressed an opinion on the alleged causal role of talc in ovarian cancer development. Dr. Kane’s opinions are mostly similar to those described by Dr. Saed, and these opinions are covered by the points I have set forth above (in B.1 and B.2). But Dr. Kane also offers two additional opinions: (1) that “[t]here is also evidence that these [talcum powder] products can be transported through the lymphatic system (Cramer 2007)” or by “inhalation leading to lymphatic transport to the ovaries (Suzuki 1991, Marchiori 2010, Frank 2011)”; and (2) that “[t]here are chemical similarities between asbestos and talc and there are striking pathological similarities between invasive serous ovarian cancer and mesothelioma.” (See, e.g., Kane Rep. at 4-5.) I explain the invalidity of these arguments as support for the hypothesis that talc powder is causally related to ovarian cancer risk in this section.

“Lymphatic transport.” Although the lymphatic transportation of inhaled topically applied talc powder could occur in rare cases, this is not relevant to the central argument that talc is carcinogenic in the ovary. If talc particles can travel through the lymphatic channel to the ovaries, they should be able to reach other human body parts and tissues as well because the lymphatic system runs throughout the body. There are no reports showing that talc is associated with other types of female (or male) cancer like colon cancer, liver cancer, stomach cancer, prostate cancer and pancreatic cancer (where lymphatic circulation is active), just to name a few. In addition, notwithstanding Dr. Kane’s suggestion that talc powder may be inhaled into the lungs as a pathway to the lymphatic system, the American Cancer Society has stated that no

increased risk of lung cancer has been reported with the use of cosmetic talcum powder, which can be inhaled during topical use in women. (See American Cancer Society official site: <https://www.cancer.org/cancer/cancer-causes/talcum-powder-and-cancer.html>.) Finally, even if talc may be present in lymphatics and lymph nodes either through skin and mucosa or by inhalation, the evidence that this mechanism can cause ovarian cancer is entirely lacking because no experimental results have demonstrated that the talc in the lymphatic vessels in fallopian tubes is present close to the ovarian cancer precursors in the fallopian tube, the origin of high-grade serous ovarian cancer. In addition, if they are carcinogenic, their presence in the lymph nodes (where the lymphatic drainage occurs) should lead to cancer in the lymph nodes (i.e., lymphoma), and there is no evidence of such a relationship.

“Chemical similarities between asbestos and talc” This is incorrect. First, talc is not asbestos. Structural similarity of chemical compounds does not mean they have the same functions or effects. For example, benzene is a well-known carcinogen that induces leukemia when a person is repeatedly over-exposed. As a result, benzene is being replaced by its many related chemical derivative compounds, like phenol and aniline. These benzene derivatives are structurally similar to benzene but they, unlike benzene, are not classified as carcinogens. Another example is estradiol, which is the most active estrogen and a known carcinogen for reproductive organ cancers in women. By contrast, both estrone and estriol are closely related to estrogen and bear structural resemblance to estradiol, but by themselves are not considered to be carcinogens. Therefore, although both talc and asbestos have structural similarity to some degree, talc is not asbestos. Second, morphological features of ovarian high-grade serous carcinoma and mesothelioma are strikingly different from the view of a board-certified pathologist, and their distinct histological features serve as the foundation for pathologists to distinguish both diseases and render correct diagnoses in the pathology reports without difficulty (although historically, prior to more advanced pathological understanding, advanced peritoneal mesothelioma may have been misdiagnosed as ovarian cancer). I have encountered numerous ovarian serous carcinomas and can attest that they bear no similarity to mesotheliomas in histopathology. Moreover, both diseases have different etiology and molecular features in their development. Therefore, Dr. Kane’s statement is totally irrelevant and reveals a misunderstanding of gynecological pathology.

C. The lack of sufficient evidence to support talc as a cause of ovarian cancer

In this part, I set forth my expert opinion on whether there is any cogent evidence showing that talc powder can cause ovarian cancer. As I explain, such evidence is lacking.

According to Merriam-Webster’s dictionary and the dictionary of NCI, a carcinogen is a substance that causes cancer. As an example, coal ash deposits have heavy concentrations of hexavalent chromium, which is a carcinogen. Carcinogens cause cancer due to their ability to damage the genome and induce cancer-driver (but not passenger) mutations that promote cancer development (Martincorena, 2017). Thus, in order to prove that any substance is carcinogenic, it is not sufficient to demonstrate exposure. One must also demonstrate that the exposure can cause biological effects and tissue/cellular changes (like precursor lesions).

As I noted above, perineal use of cosmetic talcum powder has been classified as “possibly carcinogenic to humans” by IARC (Group 2b). It should be emphasized that the term “possibly” implies uncertainty at the time when the statement was originally made by the IARC in 2010.

And further analyses of the data (including publications after 2010) have further called into question the possible carcinogenicity of talc.

The debate over whether talcum particles can cause ovarian cancer is longstanding. But despite several decades of research, the science does not support such a conclusion. Moreover, data from several studies are not correctly interpreted because of “confirmation bias” – i.e., a preference for data or conclusions that confirm rather than negate the hypothesis that talc and ovarian cancer are related. Dr. Saed’s experimental result is an example of this phenomenon.

When an unbiased review is exercised on the data that have been published in this topic, one quickly realizes that there is essentially no cogent evidence to support the suggestion that talc acts as a carcinogen in the female genital tract, including the ovary. Proof of the carcinogenic role of any agent (either biological, physical or chemical) is not a trivial undertaking; indeed, it requires robust study designs and ample samples with overwhelming consensus from the researchers in that particular field.

One example of such a robust undertaking to prove carcinogenicity involves cervical cancer, which is caused by human papilloma virus (HPV). In this case, cervical cancers and their precursors contain HPV in the epithelial cells, can be prevented by avoiding exposure to HPV or by effective immunization (HPV vaccine), are molecularly characterized by oncogenic activation by HPV particles, and can be induced by HPV oncoproteins in animal models (Roden and Wu, 2006; Roden and Stern, 2018; Sasagawa et al., 1992). This finding that HPV causes cervical cancer was awarded with the 2008 Nobel Prize of Physiology and Medicine (www.nobelprize.org/prizes/medicine/2008/press-release/). By contrast, the evidence to support the causal role of talc in ovarian cancer is conflicting, ambiguous and completely lacking from the perspective of rigorous scientific approaches. The differences in these lines of evidence are briefly summarized in **Table 1** and elaborated below.

Table 1. Comparison of HPV and perineal talc use as carcinogens in women.

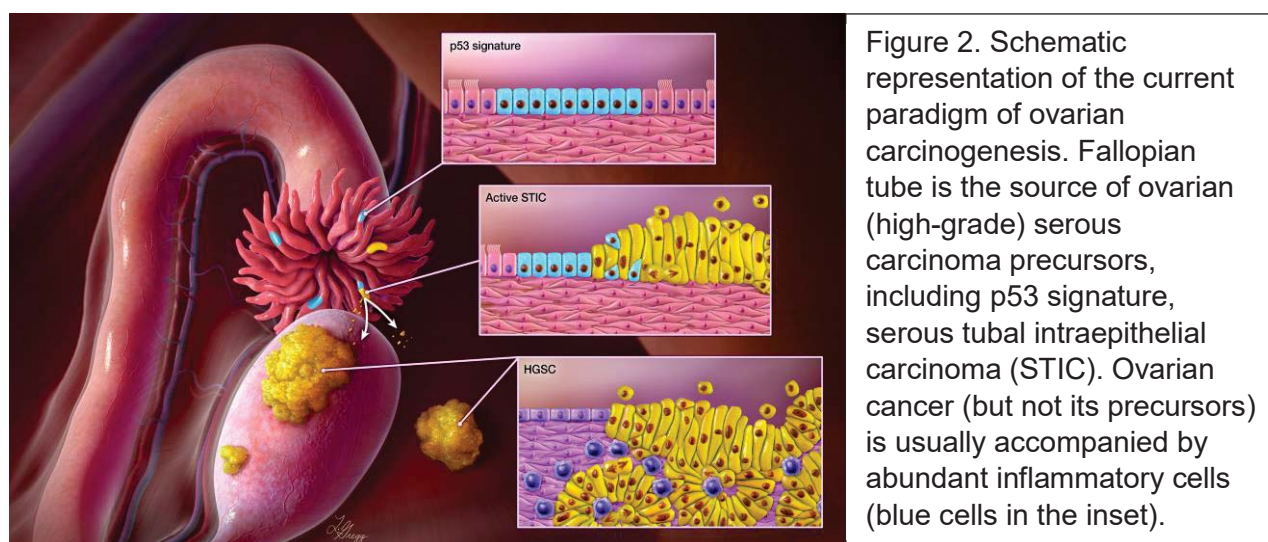
Features	HPV causes cervical cancer	Talc causes ovarian cancer
Relative risk association	Almost all are HPV associated	Equivocal; some show ~ 1.3
Present in cancer precursor lesions	Yes	No evidence of tissue reaction
Animal model(s) to support	Well established	No evidence
Molecular mechanisms	Well characterized	Not credible; with concerns

1. The new paradigm of ovarian cancer genesis – that ovarian serous carcinomas originate not in ovarian tissues, but rather in the precursor lesions in the fallopian tubes – has been widely accepted (Kurman and Shih, 2011, 2016; Kurman and Shih, 2010; Wu et al., 2018) (**Figure 2**). To claim that talc can cause ovarian cancer, one needs to not only demonstrate that talc has been deposited in the fallopian tissues,¹ but also that talc powder depositions are associated with tissue reaction, such as foreign body giant cell reaction, granulation tissues and chronic inflammation – and that those reactions then cause cancer. Talc may be inert to fallopian tube tissues, and its

¹ To confirm the presence of talc, birefringent materials would need to be identified in tissue, and those materials would need to be confirmed as talc using biochemistry or biophysical approaches.

presence should not be construed as biologically significant or related to the induction of any inflammatory response unless proven otherwise.

2. It has been established that mutations of TP53, a tumor suppressor gene, are the first molecular genetic alteration in initiating ovarian serous carcinoma in humans and such mutations are present in almost all ovarian high-grade serous carcinomas (Kuhn et al., 2012; Vang et al., 2016; Vang et al., 2013; Wu et al., 2018). TP53 mutation is also required to develop ovarian cancer in mouse models. In several published research papers, including our own (Kobayashi et al., 2015; Perets et al., 2013), inactivation of TP53 or p53 abnormality can cause ovarian cancer in mouse models. If one would like to establish the causal relationship between talc exposure and the risk of ovarian cancer, it is essential to demonstrate that talc exposures leads to TP53 mutations or inactivation. However, there is no evidence that talc exposure is associated with TP53 mutations or p53 abnormality in normal fallopian tube epithelium where ovarian cancer precursors arise. Without this direct molecular pathology evidence, a causal relationship of talc and ovarian cancer cannot be established (see below).



3. Recent advancements in genetic sequencing technology have made it possible to observe the specific changes to DNA caused by identified mutagens – and even to “tease apart the superimposed effects of several mutational exposures and processes to determine which ones occurred during the development of individual tumors” (Poon et al., 2014). Therefore, the mutation signature serves as cogent evidence that a potential carcinogen causes a certain type of human cancer. But there is a lack of such evidence showing that talc-induced/caused ovarian serous carcinomas are characterized by mutation signatures unique to those associated with talc exposures.

4. A number of epidemiological studies clearly fail to show an association between talc exposure and women who develop ovarian cancer, including prospective cohort studies (Houghton et al., 2014; Gertig et al., 2000; Gates et al. 2010; Gonzalez et al. 2016). The association between talc use in the perineal region and ovarian cancer was investigated in the Nurses’ Health Study, published by Gertig (Gertig et al., 2000) and in a follow-up study by Gates (Gates et al. 2010). “In this cohort study, arguably the strongest type of study because of its partly prospective

ascertainment of exposure, there was no association between cosmetic talc use and risk of all subtypes of ovarian cancer combined” (Langseth et al., 2007).

In another, more recent, prospective cohort study by Gonzalez et al., the authors reported that there was little association between baseline perineal talc use and subsequent ovarian cancer (HR: 0.73, CI: 0.44, 1.2). In this report, douching was more common among talc users (odds ratio: 2.1, CI: 2.0, 2.3), and douching at baseline was associated with increased subsequent risk of ovarian cancer (HR: 1.8, CI: 1.2, 2.8). The authors concluded that douching but not talc use was associated with increased risk of ovarian cancer in this study, known as the Sister Study (Gonzalez et al., 2016). In another important study reported by Nicole Urban et al., based on 74,786 Women’s Health Initiative (WHI) Observational Study (OS) participants, the authors concluded that “CA125 and HE4 contributed significantly to a risk prediction classifier combining serum markers with epidemiologic risk factors. The hybrid risk classifier may be useful to identify post-menopausal women who would benefit from timely surgical intervention to prevent ovarian cancer” (Urban et al., 2015). However, talc use is not a risk factor in both univariate and multivariate analyses (*Id.*).

In some population-based case-control studies, investigators reported a weak association between reported perineal talc exposure and ovarian cancer. The “risk association” reported in those studies should not be construed as proof of causation. A positive association is not equal to a causal relationship. Moreover, the hospital-based case-control studies did not show a statistically significant increased risk of ovarian cancer from reported perineal talcum powder use.

As an example, people who carry a lighter have a higher risk of developing lung cancer because there is an association between those who carry a lighter and the incidence of lung cancer. But it becomes apparent that it is not the lighter itself that causes lung cancer, but rather cigarette smoking (with which carrying a lighter is correlated) that is the cause. There are numerous such examples in public health topics and medical practice. The key point is that all scientists and physicians must try to establish the true cause of a disease by excluding the many confounding factors associated with ovarian cancer.

One meta-analysis (cited by Dr. Saed) is Huncharek et al., 2003. Although there appears to be a 33% increased risk of ovarian cancer in women who reportedly used perineal talc powder after meta-analysis of a total of 11,933 study subjects, the authors from this study stated (in the conclusion of the article) that “[t]he available observational data do not support the existence of a causal relationship between perineal talc exposure and an increased risk of epithelial ovarian cancer. Selection bias and uncontrolled confounding may account for the positive associations seen in prior epidemiological studies” (Huncharek et al., 2003).

Articles like these reflect the understanding by researchers that many confounding factors may exist in assessing the association between talc powder and ovarian cancer that have not yet been definitively identified.

A related problem is that the results of case control studies are prone to recall bias. This was shown in the Schildkraut study (Schildkraut et al., 2016), but could well have affected studies

before 2014 as well. Thus, even those authors who published studies finding a positive (but very modest) association between talc and ovarian cancer also cautiously mentioned the limitation of their own studies. As an example, in one very recent published paper, the authors concluded that the *“fact that the association between genital talc use and risk of ovarian cancer is present in case-control, but not in cohort studies, can be attributed to bias in the former type of studies”* (Berge et al., 2018).

In light of the limitations in the research, scientists remain skeptical of a causal connection between talc use and ovarian cancer, even if they take a precautionary approach in their own practice. A recent article relied on by plaintiffs’ experts noted that : *“[t]here is a substantial need for further research on a potential mechanism by which ovarian cancer may be caused by talc, as this will allow a causal relationship to be established or rejected with more certainty”* (Penninkilampi and Eslick, 2018). Dr. Saed’s research does not fill this void because it neither establishes nor rejects the hypothesis of a causal link between talc use and ovarian cancer.

5. Another issue concerning epidemiologic studies is that almost all reports apparently lumped all types of ovarian cancer together in their analyses. It has been well established that ovarian cancer is a highly heterogeneous group of diseases that can be broadly classified as Type I and Type II diseases (Kurman and Shih Ie, 2016; Shih and Kurman, 2004). In other words, various types of ovarian cancer are characterized by distinct clinicopathological and molecular features. Moreover, their origins and risk factors are all different.

Briefly, Type I ovarian cancers include clear cell carcinoma, endometrioid carcinoma, mucinous carcinoma and low-grade serous carcinoma. In addition to their unique histologic appearances, they are characterized by somatic mutations in PTEN, ARID1A, KRAS, PIK3CA. Both clear cell carcinoma and endometrioid carcinoma are mostly derived from previous endometriotic cysts of the ovary (or ovarian endometrioma), and the presence of ovarian endometriotic cysts carries the risk of developing both types of Type I ovarian cancer.

By contrast, Type II ovarian cancer includes high-grade serous carcinomas, the most common and aggressive type of ovarian epithelial neoplasms. Type II ovarian cancer is generally referred to as “ovarian cancer” in public because it is the most common and lethal type. In contrast to Type I ovarian cancers, high-grade serous carcinomas demonstrate a high level of proliferative activities and genomic instability, as reflected by abnormal mitoses and micronuclei. They almost all harbor TP53 mutations, but not the same type of mutations found in Type I ovarian cancers.

The risk factors of Type II ovarian cancer include the lifelong accumulated number of ovulations (so, child-bearing, oral contraceptive use and breast-feeding reduce the risk (Langseth et al., 2007)) and the germ-line mutation of BRCA1 and BRCA2 genes, which are not the same as the risks in Type I diseases. As compared to Type I ovarian cancers, the majority of Type II ovarian cancers are diagnosed late and therefore the clinical outcome of women suffering from Type II ovarian cancers can be dismal, requiring surgery and chemotherapy, and often resulting in death. Although more recently, the PARP inhibitor has been approved by the FDA to treat BRCA-mutated ovarian high-grade serous carcinomas and has been established as a

maintenance therapy in newly diagnosed advanced ovarian cancer (Moore et al., 2018), a cure for this devastating disease is still not within reach.

From this perspective, the question of whether perineal use of talc powder is related to ovarian cancer should be re-phrased more specifically as whether the talc use is associated with Type I or Type II diseases. Without specifying the tumor types in these cases, it would be difficult to start looking into this question in a scientific way. It is possible that, even if talc users have a higher than average risk in developing certain subtypes of ovarian cancer, the risk might not be the same for all types, or there is no association with some subtypes at all. If different subtypes of ovarian cancer are included as one group, it would be highly challenging to determine if talc is a carcinogen and cause of ovarian cancer or not because there are different diseases under the rubric of “ovarian cancer.”

6. The claim that talc powders can cause chronic inflammation, which can lead to the development of ovarian cancer (as proposed by Dr. Saed) is significantly flawed for at least two reasons. One is the lack of cogent evidence that talc depositions in humans are associated with chronic inflammation in normal fallopian tubes and ovaries. In a study of human ovarian tissues, researchers found no evidence of response to talc, such as foreign body giant cell reaction and/or fibrosis, and in addition found no correlation between clinical talc exposures and actual tissue talc deposition levels (Heller et al., 1996).

In experiments involving rats, applying talc powder induced genital infection (likely due to the non-sterile nature of the talc or control saline used and experimental procedure) (Keskin et al., 2009). According to the authors, no peritoneal change was observed. Thus, the forced application of talc powder into the murine genital tract artificially induced bacterial infection, which was not seen in humans, as there are no data reporting perineal talc powder use induces genital infection.

Moreover, as compared to the murine genital tract, the human fallopian tube and ovary are “far” away from the perineum. The talc powder applied to the perineal area technically needs to travel remotely to reach the fallopian tube and ovary through the vagina, cervix, and endometrial cavity. Importantly, young women who use talc powder usually have an enclosed cervix (the function of which is to prevent foreign bodies and microorganisms from coming into the uterine cavity, which is normally sterile). And even if talc powders can really arrive at the endometrial surface, the menstruation that sheds endometrial tissue off outside the body will clear these powders.

The second flaw in the inflammation theory is that if talc deposition is indeed a cause of chronic inflammation, such inflammatory background is not sufficient to cause cancer. A recent study shows that pelvic inflammatory disease (PID) was associated with an increased risk of borderline ovarian tumors, but not ovarian cancer in general. Although the results of this study suggest a histotype-specific association with PID, the association of PID with ovarian cancer risk is still somewhat uncertain and requires further investigation (Rasmussen et al., 2017). Also, in the literature, salpingitis or inflammation in the pelvis was not associated with ovarian cancer risk (Parazzini et al., 1996). Based on my own study and observation, I did not detect significant increase in chronic salpingitis in fallopian tubes containing the precursor ovarian cancer lesions. It would be critically important to the inflammation theory to associate chronic inflammation and

the occurrence of ovarian cancer precursors in the fallopian tubes – and to rule out the possibility that ovarian cancer itself induces chronic inflammation in normal tissues.

In reality, chronic inflammation observed in ovarian cancer is most likely a result of cancer, not the cause. My recent study, which is included in full at the end of this report, offers significant support for this conclusion. I reviewed samples of fallopian tissue taken from women with pre-cancerous lesions that had not yet developed into ovarian cancer, as well as from healthy women (to serve as negative controls) and from women with ovarian cancer (to serve as positive controls). My results showed that ovarian cancer precursor lesions, prior to the development of cancer, are not associated with inflammation, while ovarian cancer cases are associated with inflammation, strongly indicating that inflammation follows, but does not cause, ovarian cancer. There are several reasons why invasive carcinoma like ovarian cancer is associated with inflammatory background within cancer tissue and nearby tissue, and they include new antigens produced by the cancer cells (due to mutations) and cancer cell-induced inflammation related molecules. Because there is no evidence of this association between chronic inflammation and occurrence of tubal precursors, and, indeed, evidence to the contrary, the claim that talc deposition causes chronic inflammation, which subsequently causes ovarian cancer, is unsustainable.²

7. In any event, even assuming some role for inflammation in the development of ovarian cancer, it is important to distinguish between what is necessary and what is sufficient to cause cancer. In several human cancers, chronic inflammation is associated with the initiation of malignant changes in the tissues because of the oxidative stress that may damage DNA and cause mutations (such as TP53). Therefore, in those cancer types (such as prostate cancer and certain types of gastric cancer), chronic inflammation is required to induce tumor formation but itself is not sufficient to induce cancer development. This argument is supported by numerous reports showing that even chronic inflammation is related to cancer development; the chance to develop cancer in the chronic inflammatory background is still uncommon and most importantly, the risk is tissue type dependent. In other words, there are many endogenous and exogenous factors that can promote chronic inflammation, including aging, chronic infection and even mental stress, among others. Thus, even if there is a chronic inflammation near the ovarian precursor lesions in fallopian tubes (and in fact there is no such evidence), it still remains unclear whether this inflammation is related to talc deposition or results from other factors such as infection, aging, etc.

8. Another frequently cited study by Cibula et al. reported that tubal ligation was associated with a reduced risk for ovarian cancer (Cibula et al., 2011). The results from this study have been used by advocates who believe talc is a carcinogen to explain the blockage of talc deposition to the ovary through the fallopian tubes as a possible mechanism for the observed decrease in ovarian cancer. However, as previously mentioned, perineal use of talc powder is, at most, equivocally

² In a published report entitled “Does long-term talc exposure have a carcinogenic effect on the female genital system of rats? An experimental pilot study,” the authors concluded that “Talc has unfavorable effects on the female genital system. However, this effect is in the form of foreign body reaction and infection, rather than being neoplastic” Keskin, N., Teksen, Y.A., Ongun, E.G., Ozay, Y., and Saygili, H. (2009). *Does long-term talc exposure have a carcinogenic effect on the female genital system of rats? An experimental pilot study.* Arch Gynecol Obstet 280, 925-931.

(and inconsistently) associated with ovarian cancer risk in some retrospective case-control studies. A prospective population-based study (study of 121,700 registered nurses in the USA who were aged 30-55 years at enrollment in 1976) in the Nurses' Health Study does not identify any significant association between perineal talc use and ovarian cancer risk overall (Gertig et al., 2000). There are two alternative mechanisms accounting for the protective effect of tubal ligation. First, assuming it is true that migration of non-motile particles up the fallopian tubes is feasible, some of the ovarian cancers might be imported from the uterine cavity, where the primary tumors arise in the endometrium, and not in the fallopian tube or ovary. The tumor cells arising from the endometrium (both endometrioid and serous types) can readily travel through the fallopian tubes to reach the ovaries, which provide a suitable microenvironment for tumor cells to grow as an "ovarian" cancer. Therefore, tubal ligation can effectively block the passage of uterine cancer to the ovary. In fact, the authors on Cibula's paper also concluded in the end that the results of this meta-analysis should provide an impulse for further research on the etiology of ovarian epithelial cancers, focusing particularly on the importance of retrograde transport of endometrial cells. The other explanation is due to the surgery-induced anatomic alteration of the tubal fimbriated ends, which are no longer intimately associated with the ovulation sites of the ovary (Roy et al., 2005). Thus, the follicular fluid that is proposed to be carcinogenic (Huang et al., 2015) would not directly splash onto fallopian tube fimbrial ends, reducing the carcinogenic events of fallopian tube epithelium and preventing the occurrence of ovarian cancer precursor lesions on the fallopian tubes.

In summary, there is no relevant and cogent evidence based on the published literature, Dr. Saed's research and my own research to prove that cosmetic talc use can cause ovarian cancer. Among the steps that remain unproven are migration to the ovaries, the induction of chronic inflammation or oxidative stress, and evidence that these events are carcinogenic or precursors to ovarian cancer.

D. Undisclosed conflicts of interest affecting Dr. Saed's work

Dr. Saed testified at his deposition that he billed the time he spent preparing his manuscript to lawyers for Beasley Allen. (Saed Dep. vol. 1, 33:22-24.) The precise nature of the arrangement is unclear; he claims that his university paid for some of the lab work that was the basis for the manuscript (Saed Dep. vol. 1, 34:2-39:9), but his hours in total spent on preparing his opinion and in writing the paper are not compatible with what he was paid in sum. It is also uncertain whether Dr. Saed also disclosed his relationship with Beasley Allen to his coauthors and institution.

Regardless of the details of the arrangement, the important point is that Dr. Saed failed to adequately disclose the resulting conflict of interest. Normally, experiments and the time spent in writing research articles are part of an author's academic responsibility and are supported by research grant(s) or institutional support. To charge the time spent in preparing an article is unusual and could potentially introduce a bias into the research results. Relatedly, conflicts of interest can compromise objectivity. This can occur not only in performing the experiments but also in writing the research paper in a manner that slants toward the authors' favored conclusions.

There are indications that objectivity was compromised here. For example, it is unclear to what extent Beasley Allen influenced the design or conduct of the experiments. In his deposition, Dr. Saed was asked, “[w]ith regard to the tests that were part of the manuscript, those tests were done in connection with your communications with Beasley Allen, correct?” (Saed Dep. vol. 1, 63:9-11.) He acknowledged that he had communicated the details of his experiment to the firm, though he also insisted that the design of it was his alone. (“A. I actually designed this whole thing. So when they approached me and I got -- you know, I told them this is what I’m going to do, this is what I have in mind, we have all this setup in my lab and I want to do it, and I did it” Saed Dep. vol. 1, 67:17-21.) This insistence provides little comfort. Based on my experience in academia for 30 years, it is unusual for any scientist to communicate with a non-academic party in any form during experiments because there is no such need; thus, Dr. Saed’s departure from that norm necessarily raises questions about his motivations for sharing the details of his experiment with his financiers. It also raises a question about why the firm paid Dr. Saed for his writing of the paper since it would normally be incumbent upon Dr. Saed within the scope of his academic obligations to finish the writing and publish it himself.

One other significant indicator that Dr. Saed’s objectivity may have been compromised is the language used in the manuscript. There are a number of ways an author can write up the same results, and the choice of language can profoundly affect the general reception of the readers based on the conclusions the author chooses to emphasize and those he or she chooses to downplay or ignore. It is obvious to me, from my perspective as an author who has contributed significantly to the literature and as a frequent journal reviewer, member of several editorial boards and the prior editor-in-chief of a medical journal (*Current Obstetrics and Gynecology Report*, 2012-2015), that Dr. Saed’s paper has intentionally underscored the supposedly contributing role of talc to ovarian carcinogenesis, despite the fact that the claim is not supported by his data at all. In addition, Dr. Saed, unlike other authors, did not discuss the limitations in interpreting his results at all in the paper, which is a very unusual practice in scientific reports.

As a result, it was especially important for Dr. Saed’s conflict-of-interest statement to completely disclose the nature and purpose of his financing. Based on his deposition, I think it is clear that he did not follow best practices in scientific reporting because he failed to disclose the relationship with a law firm involved in litigation concerning the same subject matter as the manuscript, either in the conflict-of-interest statement or in his communications with the journal that has accepted his manuscript for publication.

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F. Materials Relied Upon

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Study Report to Determine Whether Chronic Inflammation Causes Ovarian Cancer

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Study location: 1550 Orleans Street, CRB-II, Rm 305, Baltimore, Maryland 21231

Time frame: 1/1/2019 to 2/11/2019

Hypothesis: Chronic inflammation has been thought to be carcinogenic in several types of human cancer including those arising from esophagus, colon, pancreas, prostate and liver. On the other hand, many cancer types are thought not to be related to chronic inflammation, including those developing from brain, connective tissue, etc. There is no evidence that ovarian cancer development is indeed caused by chronic inflammation. We hypothesize that if ovarian cancer development is caused by chronic inflammation from various etiologies, one should observe at the human tissue level that the very early lesions of ovarian cancer, i.e., ovarian cancer precursors (before ovarian cancer arises), should be accompanied by chronic inflammation in close geographical proximity to the precursor lesions.

Question to ask: To determine whether ovarian cancer precursors, especially those without concurrent ovarian cancer, are associated with chronic inflammation.

The early molecular events of ovarian carcinogenesis remain poorly understood, resulting in a lack of effective prevention and early detection strategies (Skates et al., 2017; Trabert et al., 2017). Unlike cancers arising in organs such as the colon, where the early events of carcinogenesis can be studied because their precursor lesions are well-recognized, the precursors of ovarian high-grade serous carcinoma (HGSC), the most common and lethal type of ovarian cancer, have eluded detection until recently. Accumulating evidence suggests that serous tubal intraepithelial carcinoma (STIC) or its precursor lesions, including p53 signature and serous tubal intraepithelial lesion (STIL), located at fallopian tubes or cortical inclusion cysts of the ovary, are the precursors of ovarian HGSC (Ducie et al., 2017; Kindelberger et al., 2007; Kuhn et al., 2012a; Kuhn et al., 2012b; Kuhn et al., 2012c; Kuhn et al., 2012d; Kuhn et al., 2010; Kuhn et al., 2016; Kuhn et al., 2012e; Lee et al., 2006; Lee et al., 2007; Medeiros et al., 2006; Piek et al., 2001a; Piek et al., 2001b; Sehdev et al., 2010; Vang et al., 2012b; Visvanathan et al., 2017). The reported incidence of tubal lesions varied in the literature, but when a rigorous sampling was performed in a large cohort of fallopian tubes from a high-risk population, the incidence of p53 signature and STIC/STIL can be as high as 27% and 12%, respectively (Visvanathan et al., 2018).

Microscopically, STICs exhibit significant nuclear atypia and architectural alterations, *TP53* mutations and high proliferative/apoptotic activity. STIC cells are often loosely arranged and can readily disseminate outside the fallopian tube. The p53 signature is identified as a stretch of 12-30 normal-appearing epithelial cells having a p53 immunoreactivity pattern compatible with a missense *TP53* mutation and displaying low proliferative activity, similar to adjacent normal tubal epithelium. The term STIL has been used to describe, among other lesions, a group of tubal precursors characterized by lower levels of nuclear atypia than STIC, p53 staining patterns

compatible with either missense or deleterious TP53 mutations, and a level of proliferative activity similar to adjacent normal epithelium (Vang et al., 2012a; Visvanathan et al., 2011). “Dormant STICs” in this study were deemed morphologically compatible with STILs by a panel of gynecologic pathologists. Although molecular relationships between STICs and concurrent ovarian HGSCs have been reported (Eckert et al., 2016; Kuhn et al., 2012b; McDaniel et al., 2015; Rabban et al., 2015; Singh and Cho, 2017; Visvanathan et al., 2017), few of these studies analyzed p53 signatures or STILs, largely because of technical challenges. More importantly, since all of these studies analyzed patients with tubal lesions co-existing with advanced ovarian HGSCs, it is likely that some of these lesions were disseminated tumor cell clones from the adjacent, concurrent ovarian tumors, therefore obscuring the evolutionary histories. This issue is aggravated in ovarian HGSCs, which are often diagnosed late, at which time the vast late-stage tumor mass overwhelms or effaces the precursor lesions located at either the fallopian tube or the small cortical inclusion cysts of the ovary, leaving little trace of the molecular landscape existing before the advent of invasive cancer. Indeed, a recent article cautioned against clonal evolution studies performed on advanced tumors with high genetic heterogeneity and the possibility of constituent clones arising from multiple cell lineages (Alves et al., 2017). Consequently, distinguishing between true precursor lesions and HGSC implants is problematic (Rabban et al., 2015; Singh and Cho, 2017). Nevertheless, powerful techniques for analysis of clonal evolution are useful for assessing clonal relationships between primary tumor and distant metastases and when true precursor lesions are available, the same tools can provide similarly powerful means to delineate tumor evolution (Wu et al., 2018).

Study design and case selection: The cases were retrieved from the archival files from the ovarian cancer precursor registry supported by the US Department of Defense (USAMRMC), Directed Medical Research Programs (CDMRP), grant title: “Prevention of Ovarian High-Grade Serous Carcinoma by Elucidating Its Early Changes,” grant number: W81XWH-11-2-0230. The purpose of this completed study is to determine the origin and pathogenesis in the development of ovarian high-grade serous carcinomas by employing cancer genetics, cell biology, animal models and epidemiologic studies through a multi-institutional research effort. The consortium includes five research projects and three cores. Tissue collection started as early as 2013. This archival file contained 48 cases of ovarian cancer precursors, carcinoma and normal fallopian tubes, and their diagnoses were made after a prior pathology review by a panel of gynecologic pathologists. Many research projects have utilized this and its related resources (please see the attached information), resulting in peer-reviewed publications. This indicates that this tissue source is useful and reliable to study projects related to ovarian cancer pathogenesis.

In particular, I identified the cases showing ovarian cancer precursor lesions without concurrent ovarian cancer. I also selected a few cases of ovarian cancer as the controls. I excluded those cases showing active bleeding (the presence of inflammatory cells due to hemorrhage can confound the interpretation). Once identified, I retrieved the slides, including H&E, and accompanied immunostaining slides. All cases are anonymous, without patients’ personal identifiers (but labeled with experimental ID). I re-reviewed and recorded results and took representative photomicrographs using a Nikon Eclipse Ci light microscopy and Nikon digital camera. Images were taken at either 20X or 40X when appropriate. A total of 59 lesions and areas of interest from 48 individuals were included in this study. The review of the slides took place in the Cancer Research Bldg,- II, Room 305 at the Johns Hopkins Medical Institution,

Baltimore, Maryland, from February 2 to February 18, 2019.

Diagnosis criteria: I used the criteria to diagnose ovarian cancer precursor lesions as summarized in the research papers of which I am one of the coauthors (Vang et al., 2012a; Visvanathan et al., 2011). To determine if the precursor lesions are associated with chronic inflammation, I use lymphocyte infiltration in the stroma and or within the epithelium of the lesion on either H&E stained or immunohistochemically stained slides. To better demonstrate chronic inflammation in tissues, I also used positive control slides showing increased lymphocytic infiltrate as the references. To conclude that there is a chronic inflammation, I must observe a significant increase in lymphocyte density within the lesion or in its immediate stromal tissue as compared to the background normal-appearing fallopian tube epithelium without precursor lesions or carcinomas. Alternatively, fused plicae of the fallopian tube papillae can also be considered as evidence of prior salpingitis (chronic inflammation in fallopian tube) in appropriate cases. To compare the lymphocyte density between lesion and normal epithelial areas is important, as there is a normal immune surveillance in normal fallopian tube mucosa containing the resident immune cells, including lymphocytes (Ardighieri et al., 2014). I diagnose chronic inflammation based on my training as a pathologist and experience practicing gynecologic pathology for 20 years. The criteria used here is no different from those in my clinical practice.

Research findings: After identifying those qualified cases, I organized them into individual slide holders (one case in one folder). First, I used the low-power lens (4X) to look for the regions of interest, followed by higher-power lenses, including 10X, 20X and 40X on H&E slides. For p53 signature cases, I used p53 antibody stained slides since the H&E stain will not allow one to identify p53 signatures. I recorded the diagnosis and evaluated the density of chronic inflammatory cells, i.e., lymphocytes on the slides on H&E and/or immunostained slides. I compared the lymphocyte density between the lesion and the background normal-appearing fallopian tube mucosa. I then took photomicrographs on the lesions or regions of interest (usually at 20X) and saved the image files as .jpg files in my desktop computer in a folder. I labeled the file names of each image using the original experimental ID to avoid confusion.

My study result was summarized in the following **Table 2**. A total of 59 areas of interest were analyzed, and they included 18 p53 signature lesions, 25 STICs, eight normal fallopian tubes and eight ovarian (high-grade) serous carcinomas. Based on intraepithelial and intra-stromal lymphocyte density, as well as the architecture of tubal plicae, I did detect chronic inflammation in carcinoma tissues (the positive controls). When I applied the same criteria, I did not observe chronic inflammation in the p53 signatures and STIC lesions as compared to their background normal-appearing fallopian tube mucosa in any of the cases examined. **The photomicrographs are attached as an appendix**, and one can see that there are two types of images presented. One is conventional H&E slides to show the STICs and the other is immunohistochemistry (mostly p53 staining) to demonstrate p53 signatures, because without p53 staining, p53 signature lesions could not be identified by H&E staining. Immunohistochemistry using immune cell markers was not performed because it is not required to do so in routine diagnostic pathology, although chronic inflammation can be validated by immunostaining to highlight immune cells. Although not required, every board-certified anatomic pathologist now learns how to perform this procedure as part of his or her training. I also focused on comparing the lymphocyte density

between a lesion and its immediately adjacent normal region whenever the junctions were available for study. As a result, I did not see the difference between the lesion and the adjacent normal areas in terms of increased level of lymphocytic infiltration. Besides, there is a heterogeneity of lymphocyte density within normal fallopian tube mucosa with unknown significance; therefore, I used the average of lymphocyte density from normal fallopian tube mucosa to compare to those in fallopian tube precursor lesions.

In this study, I also ask whether there is any difference in lymphocyte density in mucosae (the connective tissue layer beneath the tubal epithelium) between normal fallopian tubes and those fallopian tubes harboring ovarian cancer precursor lesions (but without ovarian cancer). For the former, I selected eight new cases (10028, 10031, 10039, 10052, 20001, 20001, 20003, 20004), together with 10 previously reported cases (Ardighieri et al., 2014) (for a total of 18 normal-appearing fallopian tubes). As a result, there is no evidence that either group has an apparent increase in lymphocytes in mucosae. Like the fallopian tubes harboring precursor lesions, normal fallopian tubes do not have chronic inflammation.

Interpretation and Discussion: Based on the data presented, I attest that ovarian cancer precursor lesions, including STIC and p53 signatures (before cancer develops), are not associated with increased lymphocyte infiltration, and thus there is no evidence of chronic inflammation. This new result refutes the hypothesis that chronic inflammation can cause the malignant transformation of fallopian tube epithelium into cancer precursor lesions. If the precursor lesions are not the result of chronic inflammation, ovarian cancer is not caused by chronic inflammation because ovarian cancer (the invasive cancer) must derive from its precursor (i.e., p53 signatures and STICs), just like all other human cancers. Similarly, a recent study published by Malmberg et al. did not find evidence that chronic inflammation or tubal injury is involved in the carcinogenesis of ovarian cancer (Malmberg 2016).

Unlike cancers arising in organs such as the colon, where the early events of carcinogenesis can be studied because their precursor lesions are well-recognized, the precursors of ovarian high-grade serous carcinoma (HGSC), the most common and lethal type of ovarian cancer, have eluded detection until recently. Accumulating evidence suggests that serous tubal intraepithelial carcinoma (STIC) or its precursor lesions, including p53 signature and serous tubal intraepithelial lesion (STIL), located at fallopian tubes or cortical inclusion cysts of the ovary are the precursors of ovarian HGSC (Kurman and Shih Ie, 2016; Kurman and Shih, 2010) (Wu et al., 2018). The reported incidence of tubal lesions varied in the literature, but when a rigorous sampling was performed in a large cohort of fallopian tubes from a high-risk population, the incidence of p53 signature and STIC/STIL can be as high as 27% and 12%, respectively (Visvanathan, 2018).

One may ask why this study focuses on determining the chronic inflammation in precursor lesions rather than in ovarian cancer. This is because if the study analyzed patients with tubal lesions co-existing with advanced ovarian high-grade serous carcinomas, it is likely that some of these lesions were indeed the disseminated tumor cell clones from the adjacent, concurrent ovarian tumors, therefore obscuring the evolutionary histories. This issue is aggravated in ovarian HGSCs, which are often diagnosed late, at which time the vast late-stage tumor mass overwhelms or effaces the precursor lesions located at either the fallopian tube or the small

cortical inclusion cysts of the ovary, leaving little trace of the molecular landscape existing before the advent of invasive cancer. More importantly, cancer often induces chronic inflammation due to the neo-antigens (due to many missense mutations that produce new epitopes of proteins) that trigger immune responses in tissues. In this case, it is unknown if the chronic inflammation associated with cancer is the cause of the cancer or the result of it. All things considered, the best experimental approach is to directly observe the precursor lesions and detect if chronic inflammation is present. If yes, the development of ovarian cancer can be causally induced by chronic inflammation. Otherwise, the chronic inflammation that always occurs in ovarian cancer is not the cause of carcinogenesis of ovarian carcinoma. So, the final answer from this study is that ovarian cancer precursor lesions are not associated with chronic inflammation, thus refuting the hypothesis that chronic inflammation is the cause of ovarian cancer.

In conclusion, the most plausible cause of ovarian (high-grade) serous carcinoma is related to the incessant ovulation theory, which posits that the accumulated numbers of ovulations increase the risk. This risk is substantially further enhanced by genetic predisposition, including BRCA1/2 germline mutations. Temporary cessation of ovulation, such as during pregnancy or while taking birth control, is known to have a significant protective effect with respect to ovarian cancer (Bera, 2008), and the mechanism of this effect is revealed by recent advances in this study field. Previous studies have examined the link between ovulation and cancer development by examining fallopian tube follicular fluid (FF), which bathes fallopian tubes after each ovulation and is a required process during ovulation (Bahar, 2014) (Hsu, 2015). Scientists found that FF in high concentrations could cause significant DNA damage, double-stranded breaks, and TP53 nuclear accumulation that created an immunostaining pattern similar to that seen in p53 signature. Reactive oxygen species (ROS) and the IGF2 have been implicated in this mutagenesis (Hsu, 2015) (Hsu, 2019).

Lesion	case ID	diagnosis	with concurrent cancer	inflammation*
1	S80001	p53 sig	no	no
2	S80002	p53 sig	no	no
3	S80003	STIC	no	no
4	S80004	p53 sig	no	no
5	S80005	p53 sig	no	no
6	S80006	p53 sig	no	no
7	S80007	STIC	no	no
8	10150	STIC	no	no
9	10149	p53 sig-1	no	no
10	10149	p53 sig-2	no	no
11	10148	p53 sig	no	no
12	10147	STIC	no	no
13	10146	STIC	yes	no
14	10146	ovarian cancer	yes	yes
15	10145	p53 sig	no	no
16	10144	STIC	no	no
17	10142	p53 sig	yes	no
18	10142	ovarian cancer	yes	yes
19	10141	STIC	yes	no
20	10141	ovarian cancer	yes	yes
21	10137	STIC-1	no	no
22	10137	STIC-2	no	no
23	10136	STIC	no	no
24	10135	STIC	no	no
25	10133	STIC	no	no
26	10060	STIC	no	no
27	10059	STIC	no	no
28	10058	ovarian cancer	yes	yes
29	10058	STIC	yes	no
30	10057	ovarian cancer	yes	yes
31	10056	STIC	no	no
32	10055	ovarian cancer	yes	yes
33	10053	STIC	yes	no
34	10013	STIC-1	no	no
35	10013	STIC-2	no	no
36	10013	STIC-3	no	no
37	10013	p53 sig	no	no
38	30032	STIC	no	no
39	20073	STIC	no	no
40	10046	p53 sig	no	no
41	20055	ovarian cancer	yes	yes
42	20055	STIC	yes	no
43	10022	p53 sig	no	no
44	10020	p53 sig	no	no
45	10043	p53 sig	no	no
46	10018	p53 sig	no	no
47	10026	p53 sig	no	no
48	10013	p53 sig	no	no
49	20114	STIC	yes	no
50	20114	ovarian cancer	yes	yes
51	10011	STIC	no	no
52	10028	NFT	no	no
53	10031	NFT	no	no
54	10039	NFT	no	no
55	10052	NFT	no	no
56	20001 NFT	NFT	no	no
57	20002 NFT	NFT	no	no
58	20003 NFT	NFT	no	no
59	20004 NFT	NFT	no	no
*Inflammation is defined by increased lymphocytic infiltrate associated with the lesions as compared to the background normal tissues or mucosa.				

Table 2. The summary of the results.

Appendix

Publications supported by DoD Ovarian Cancer Consortium (OCPR: W81XWH-11-2-0230)

Title: Prevention of Ovarian High-Grade Serous Carcinoma by Elucidating Its Early Change
2011-Current (all investigators in this consortium)

6.1. Journal publications (with acknowledgement of federal support)

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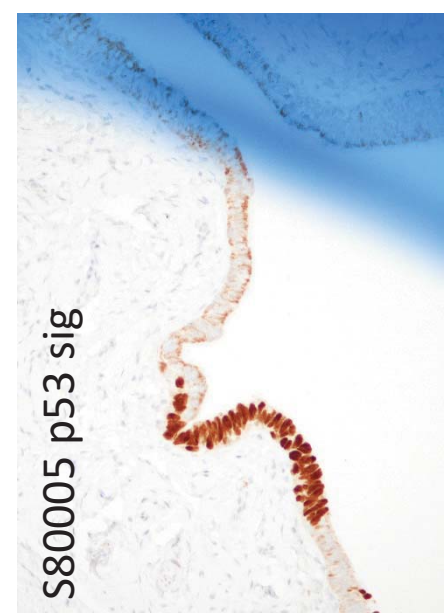
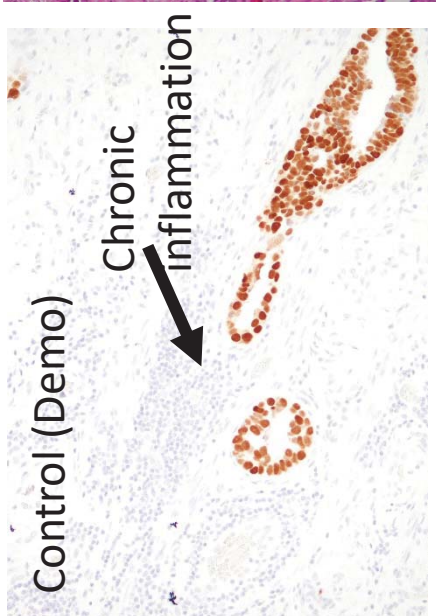
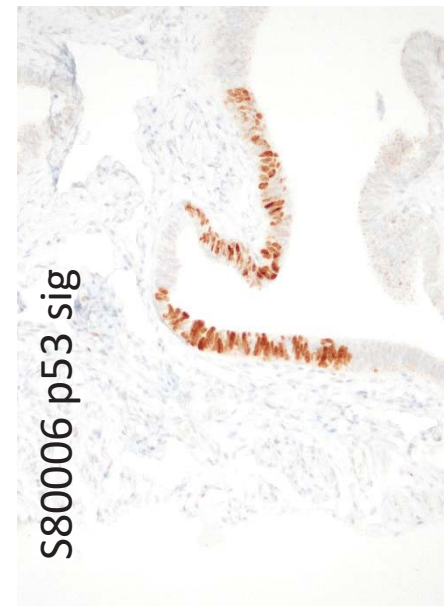
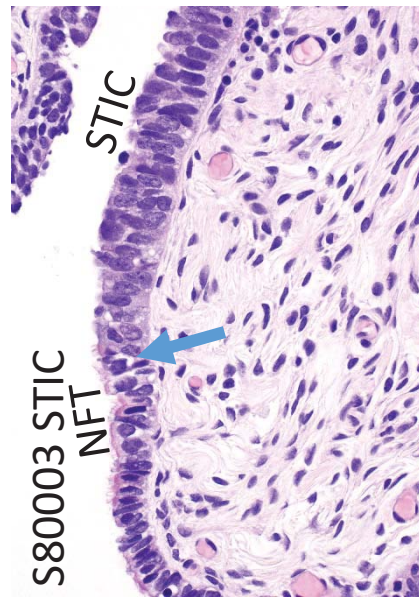
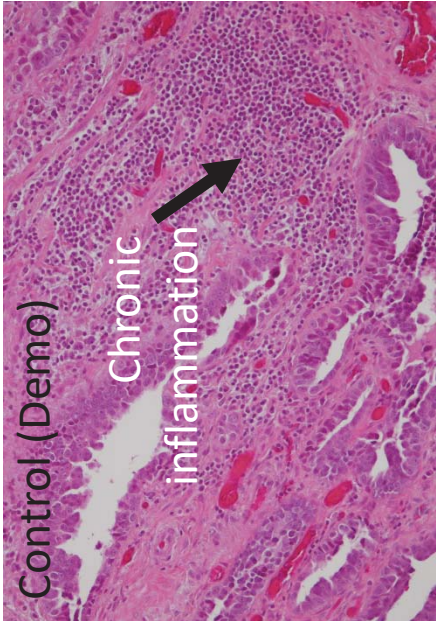
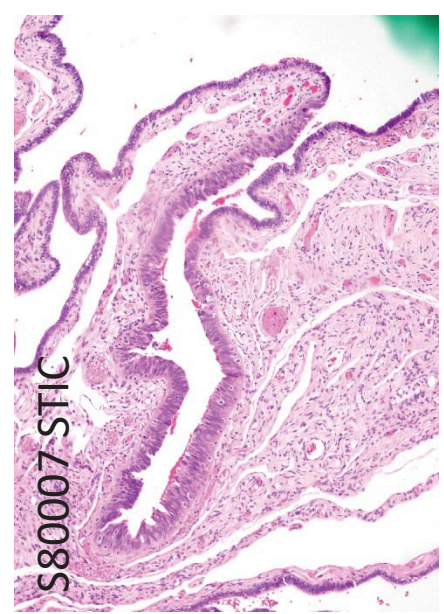
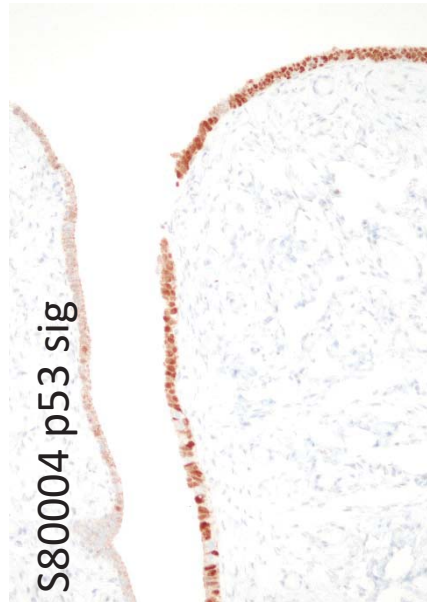
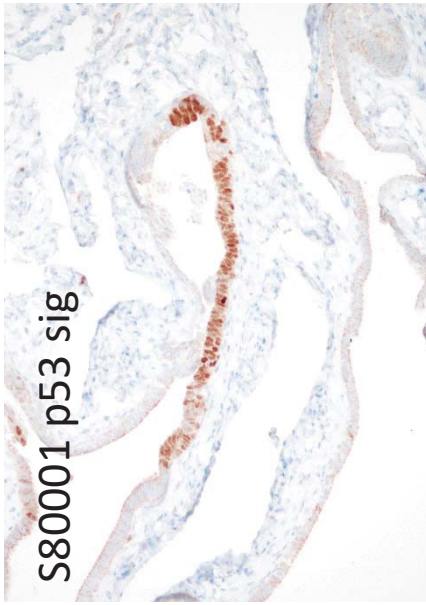
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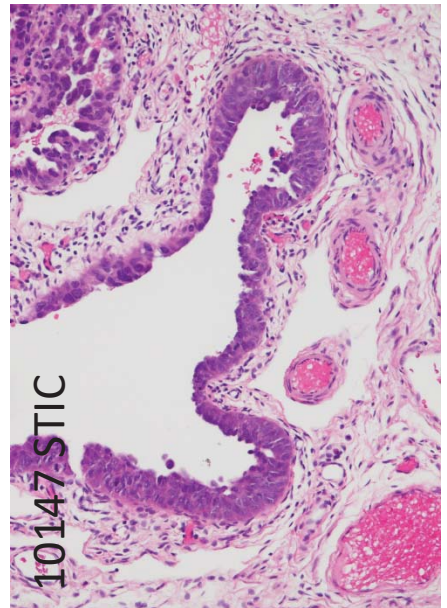
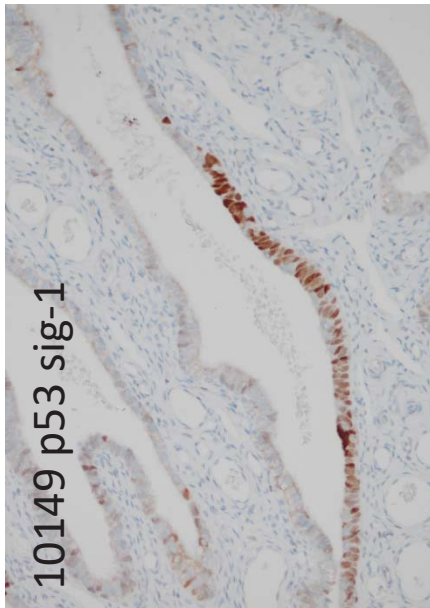
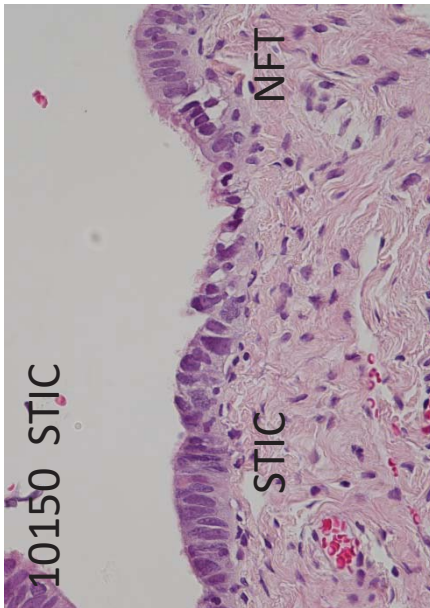
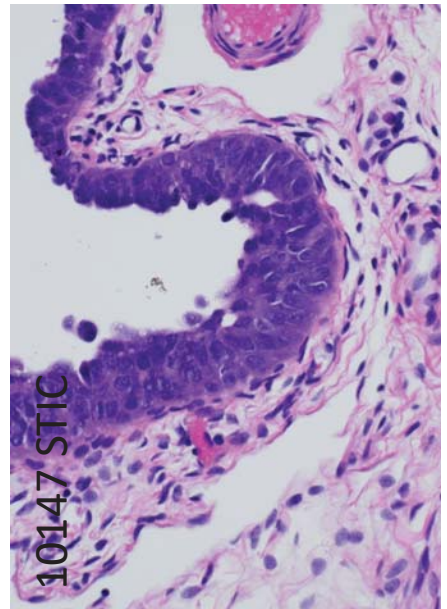
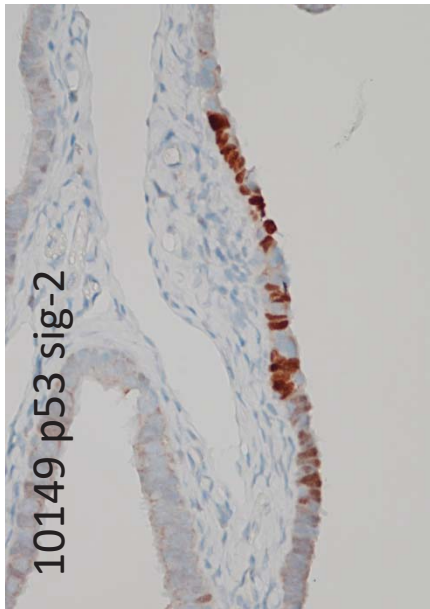
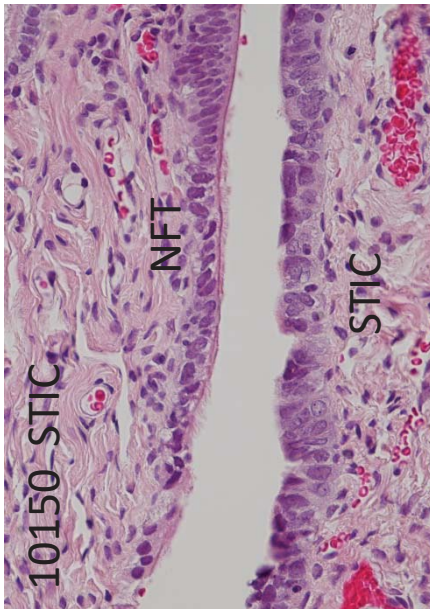
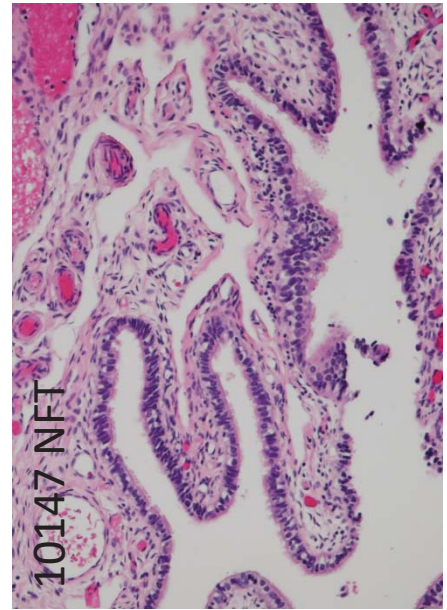
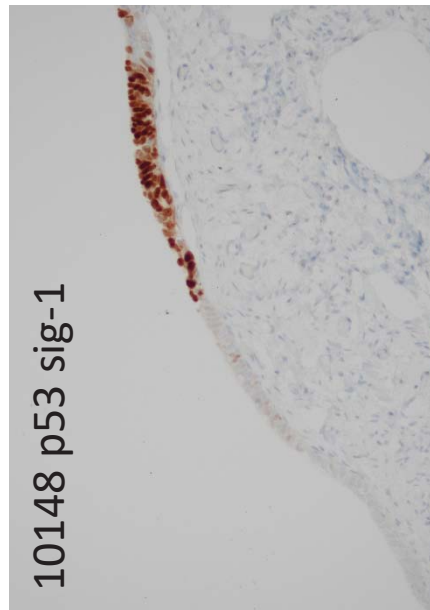
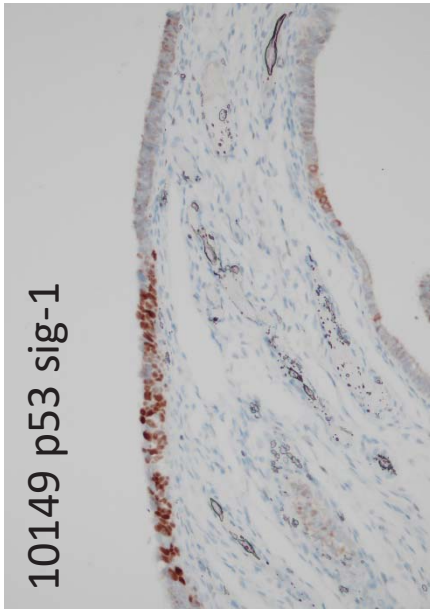
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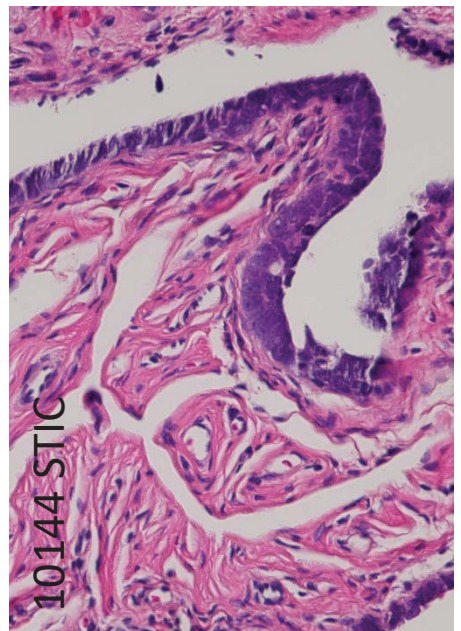
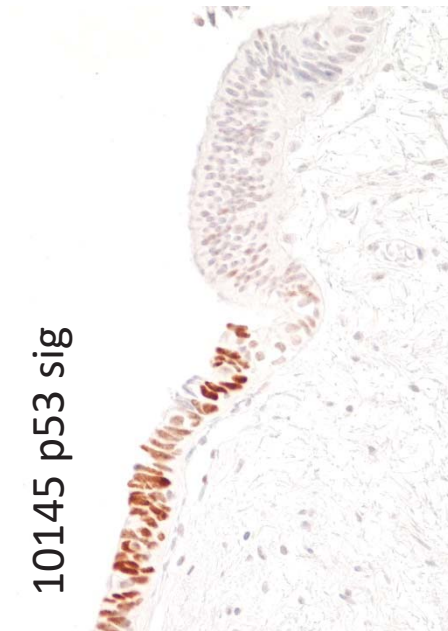
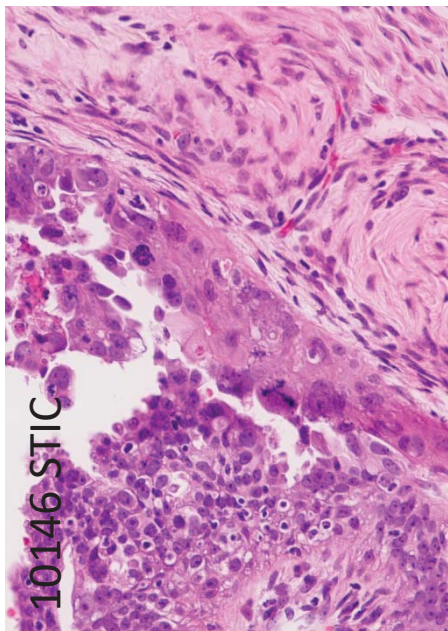
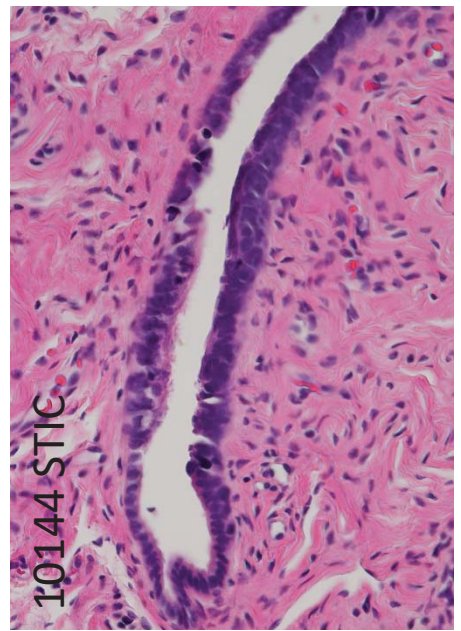
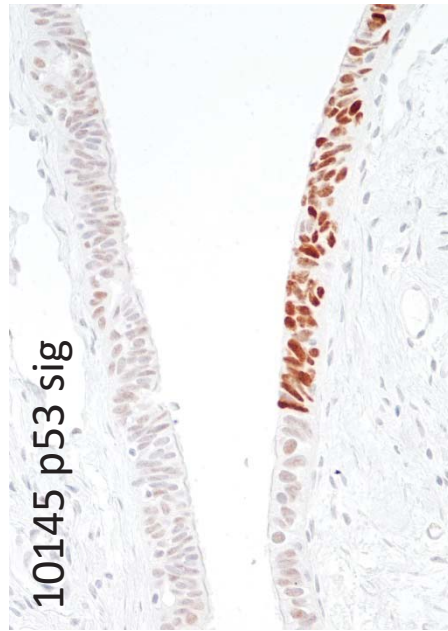
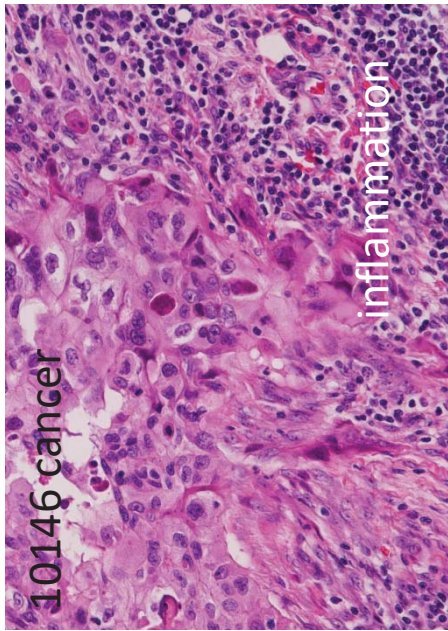
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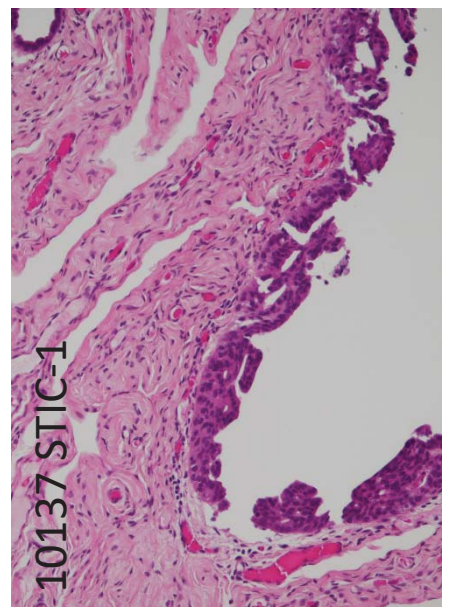
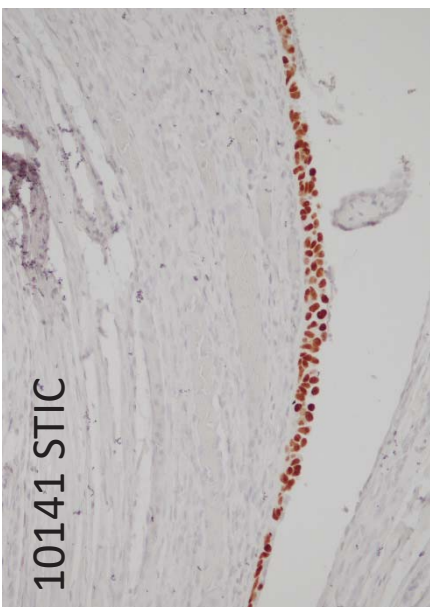
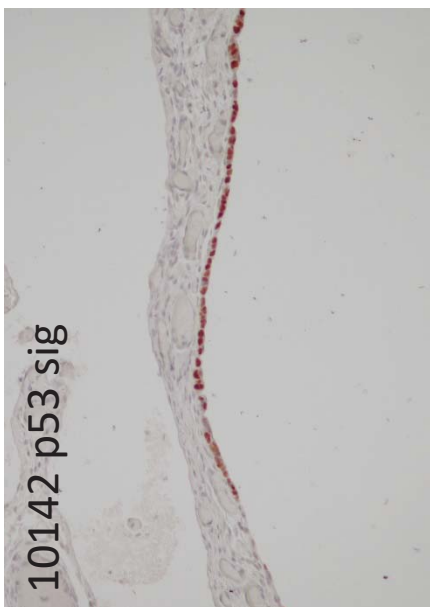
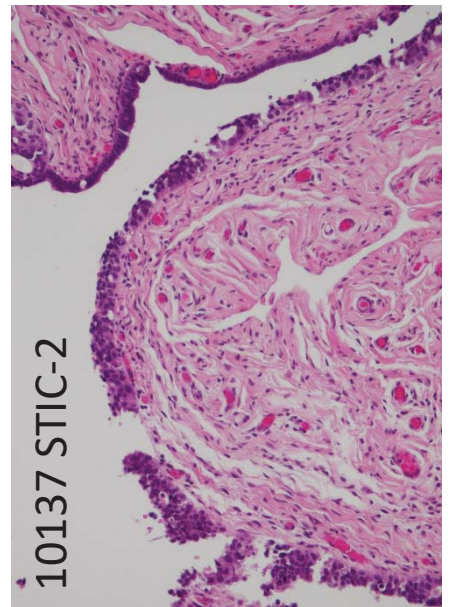
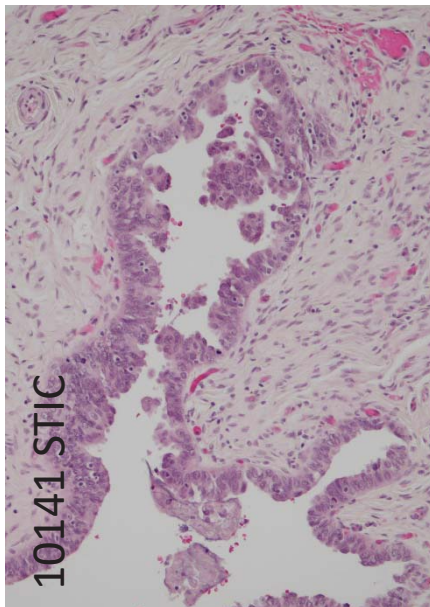
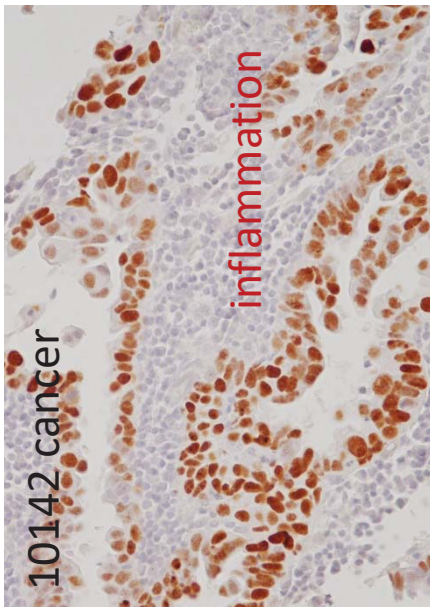
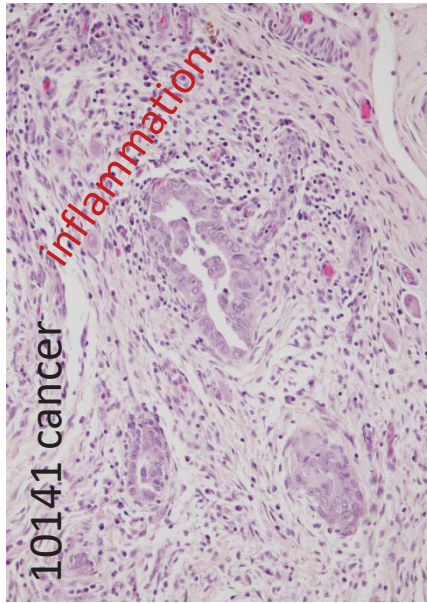
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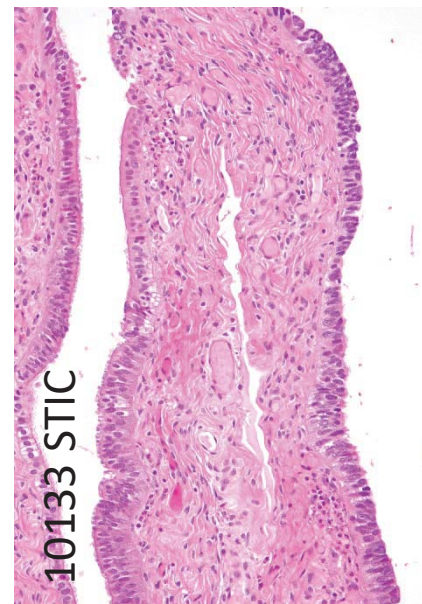
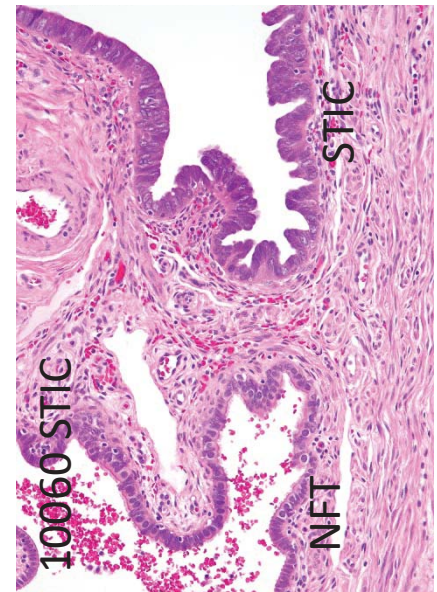
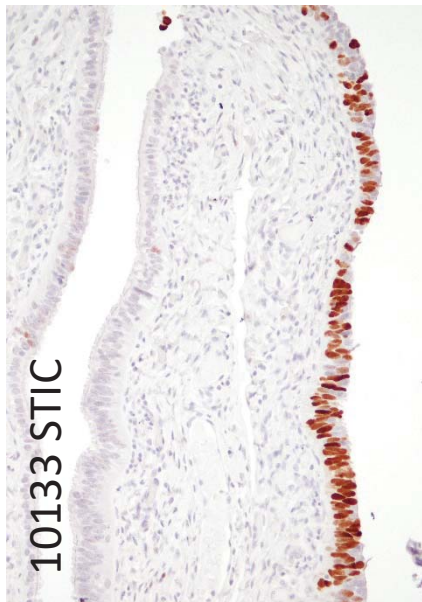
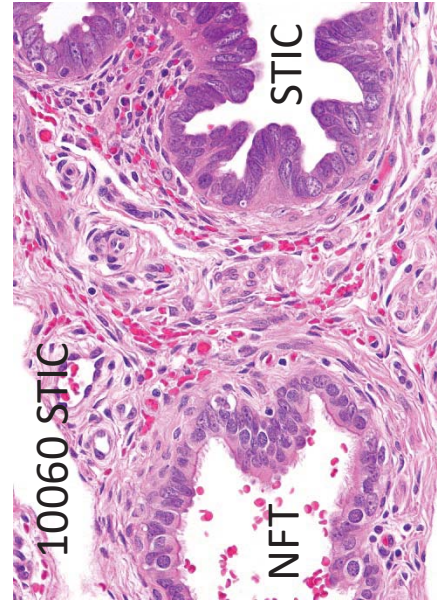
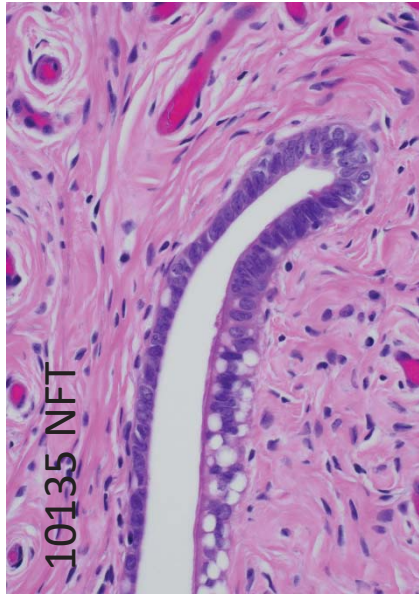
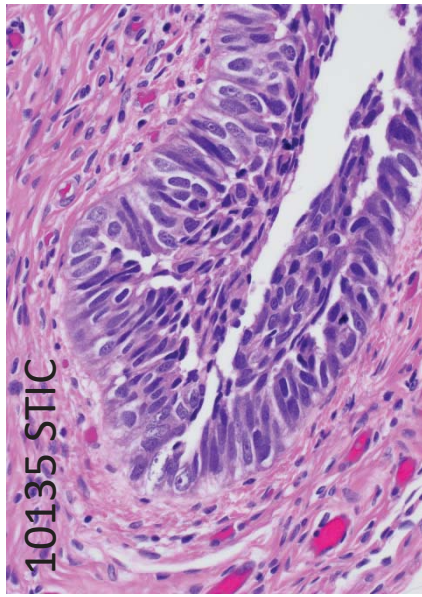
Appendix: Photomicrographs

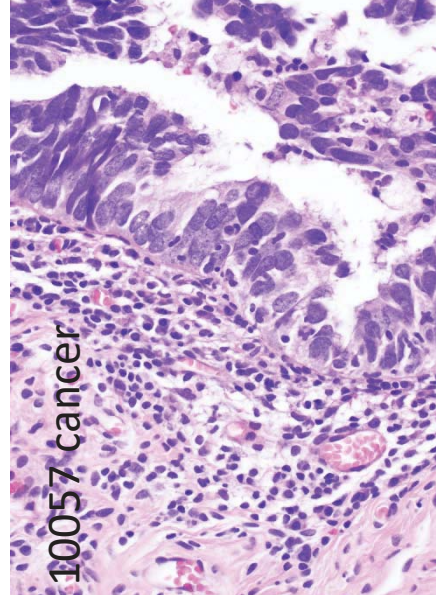
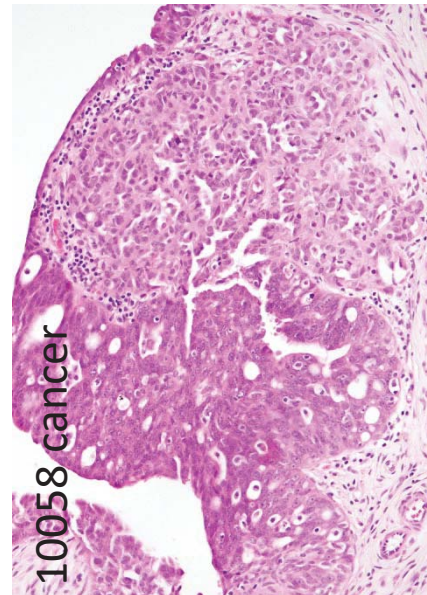
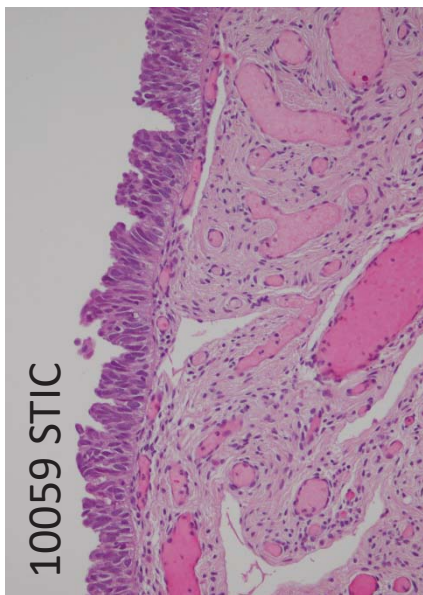
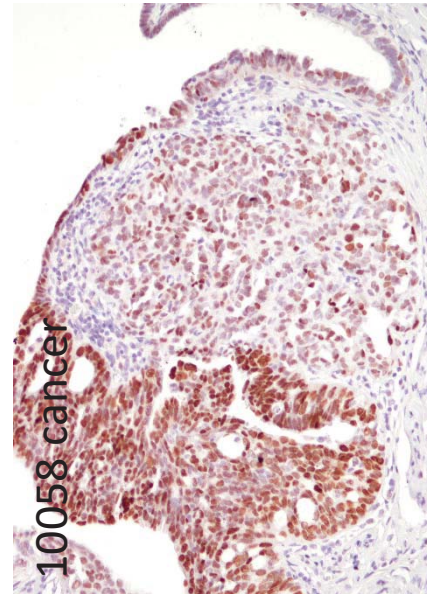
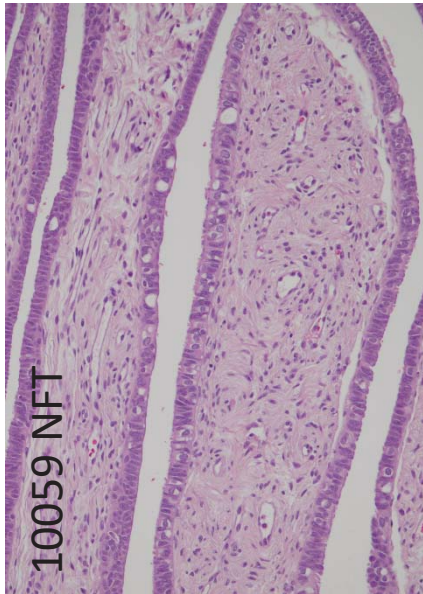
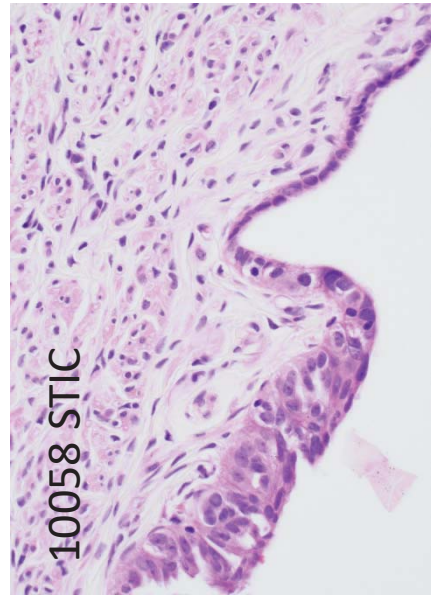
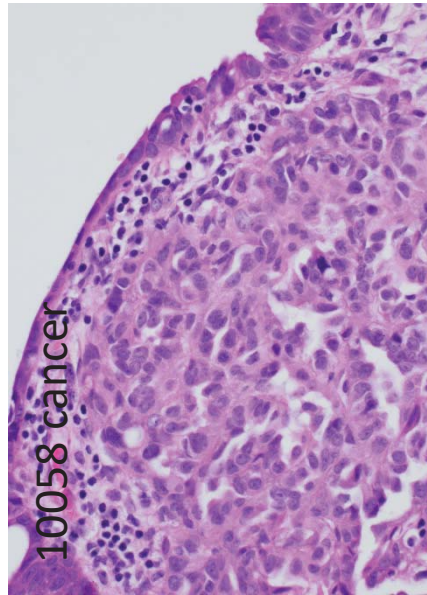
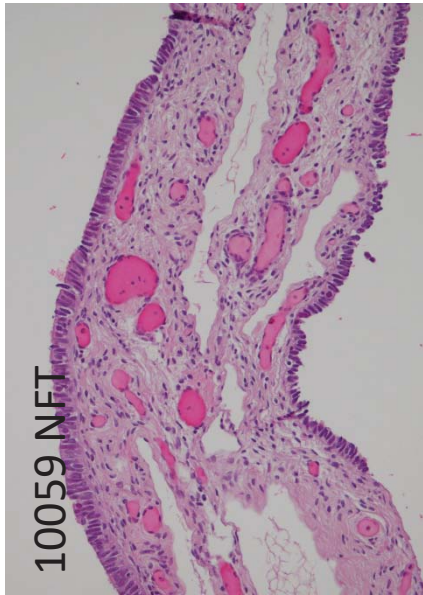


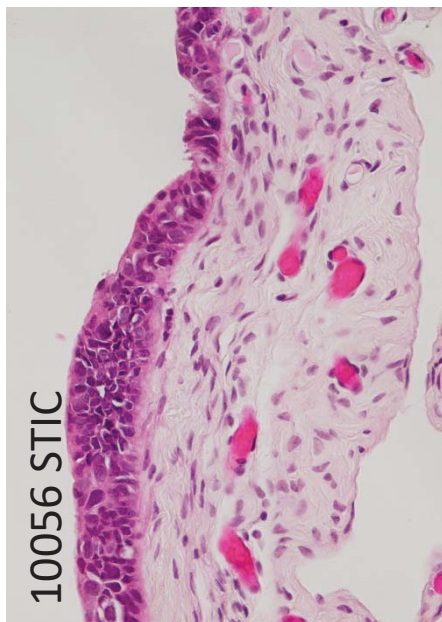
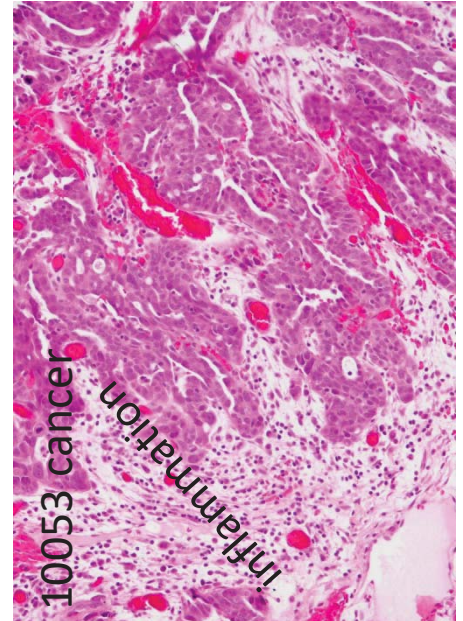
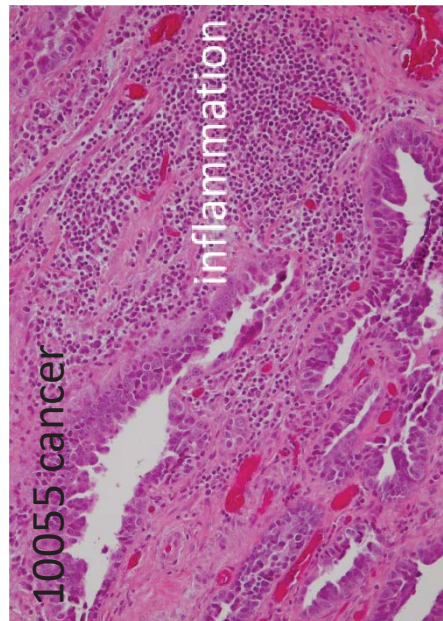
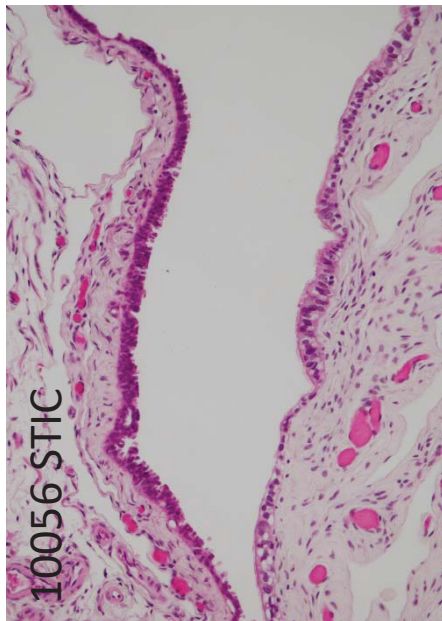




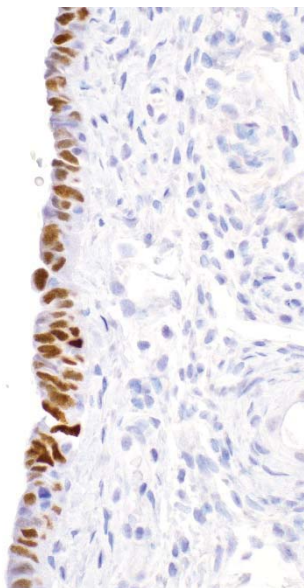




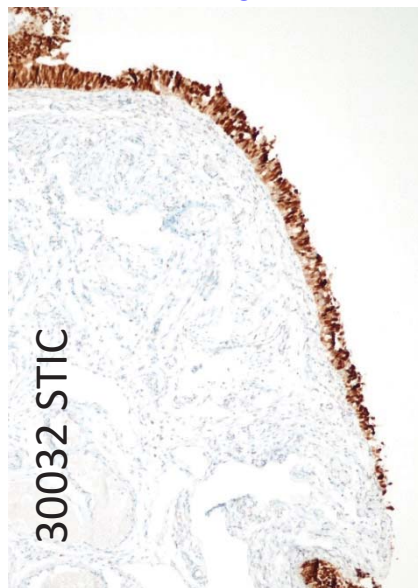




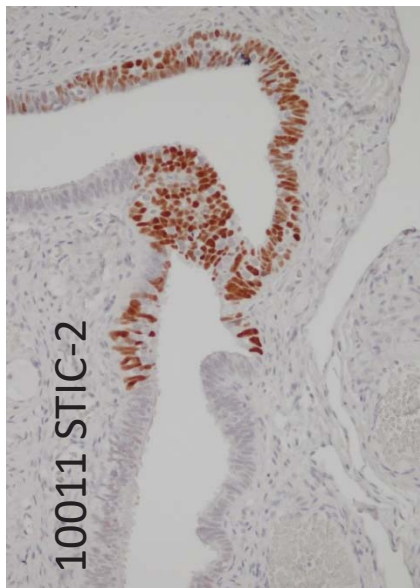
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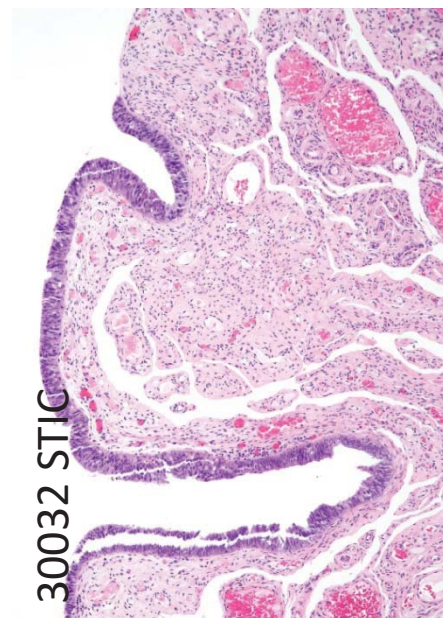
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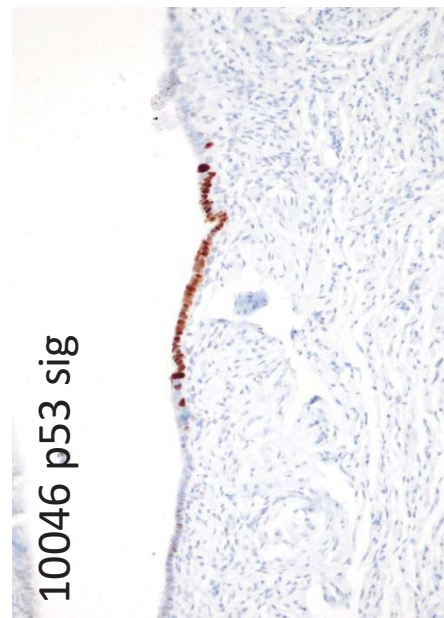
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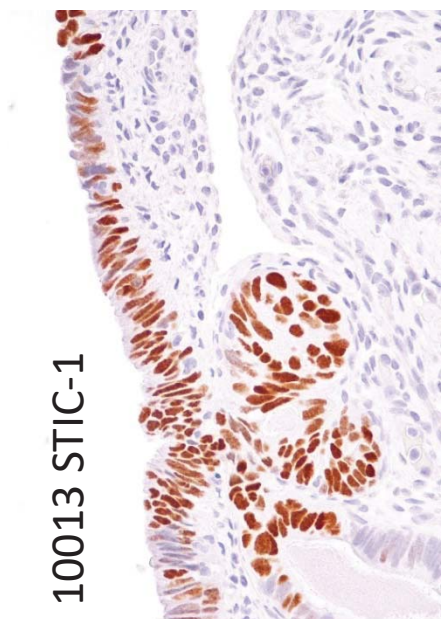
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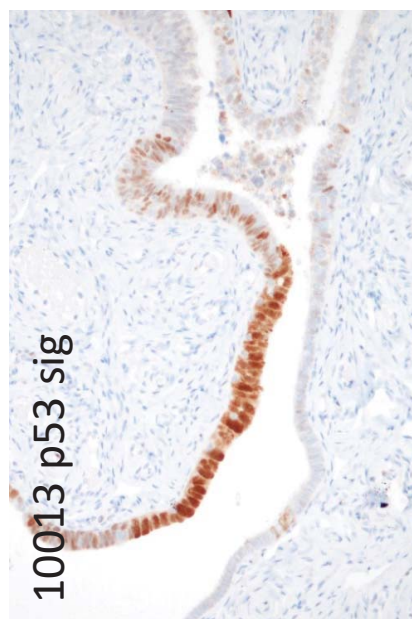
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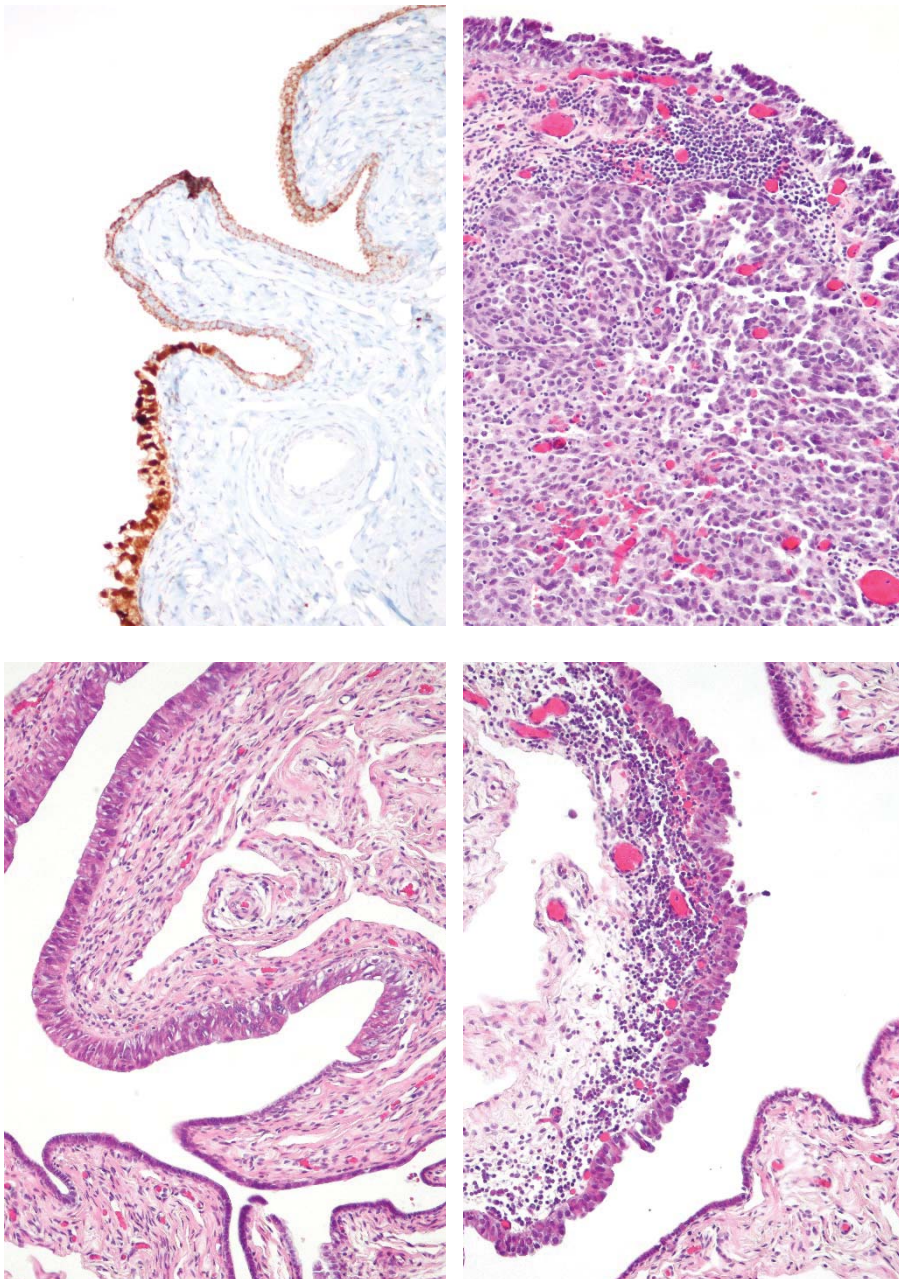
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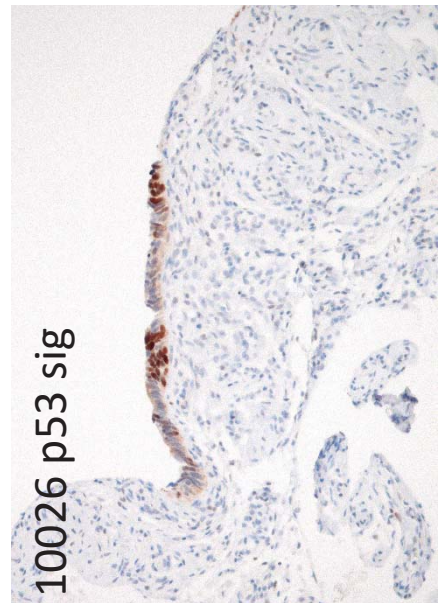
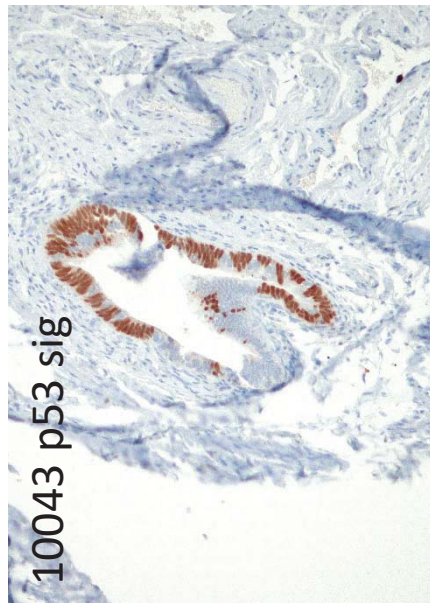
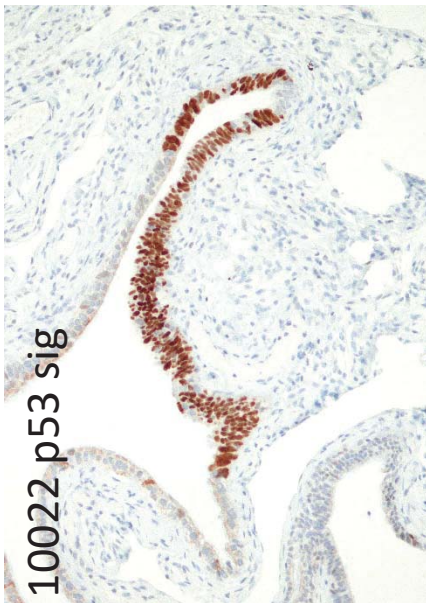
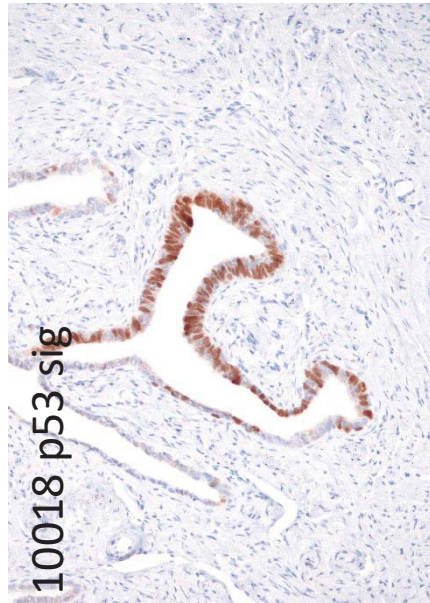
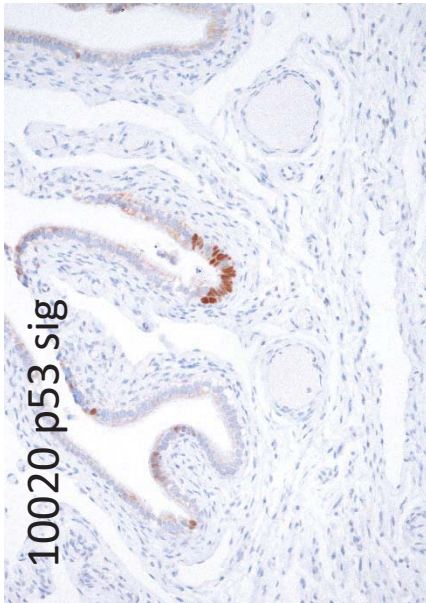


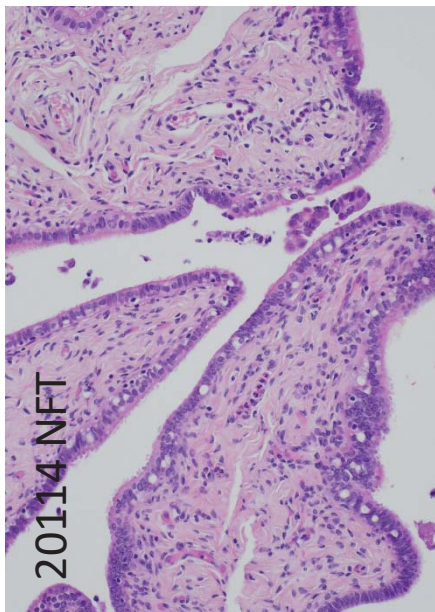
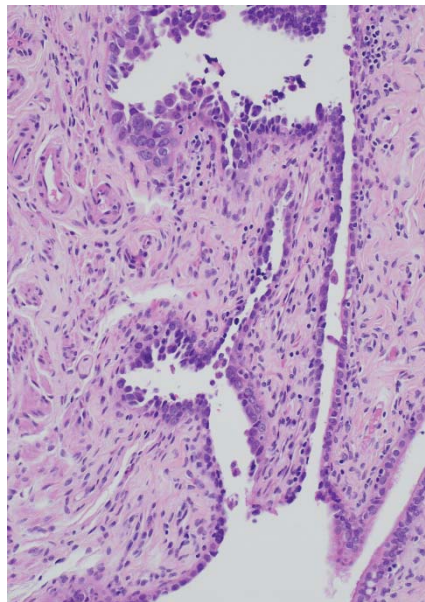
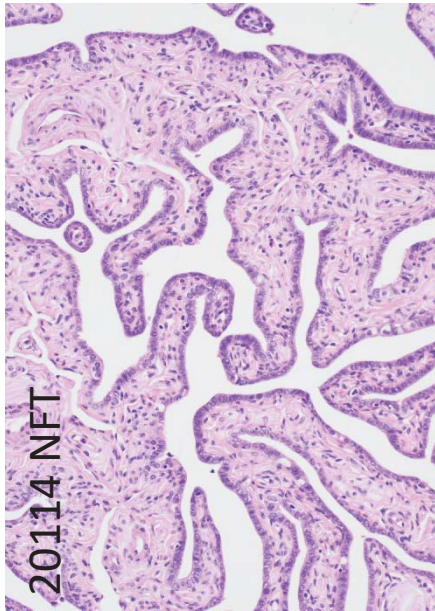
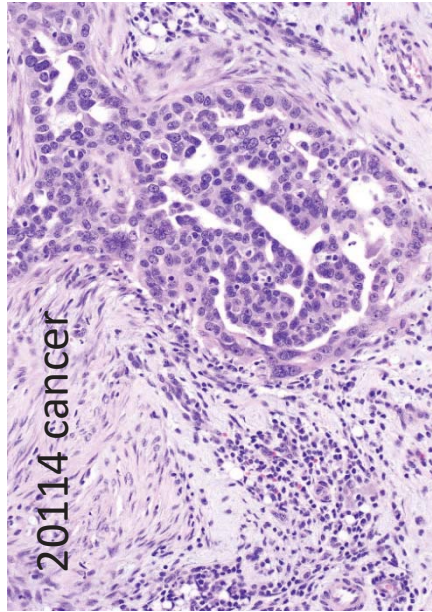
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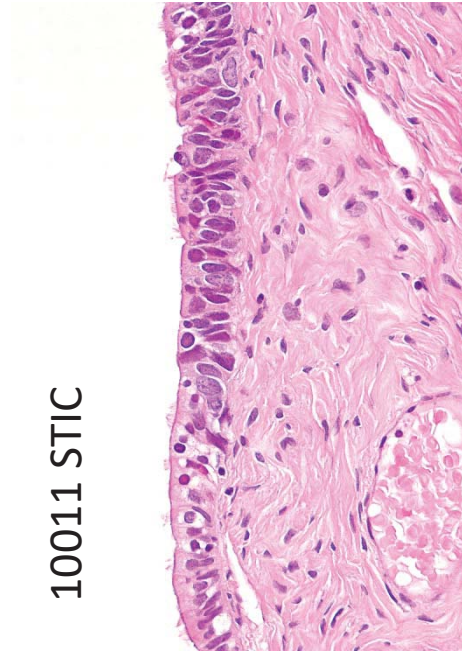
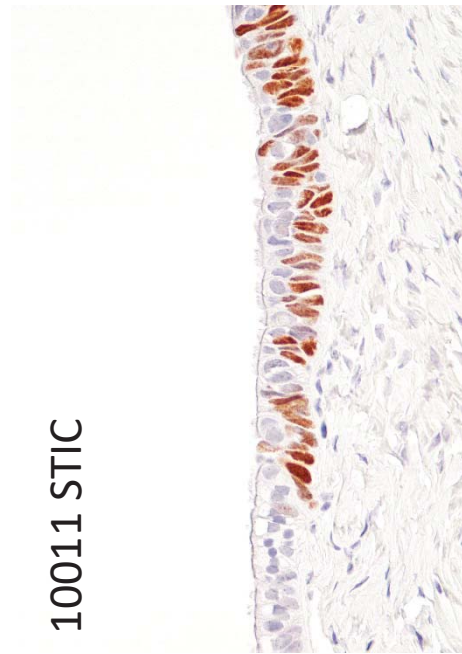


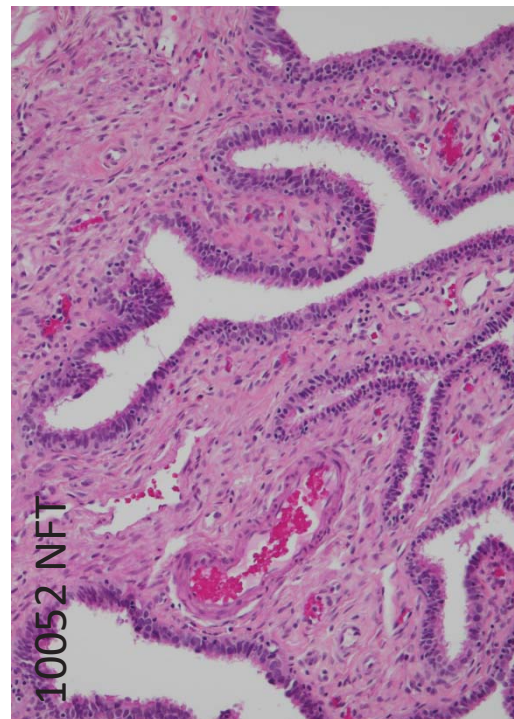
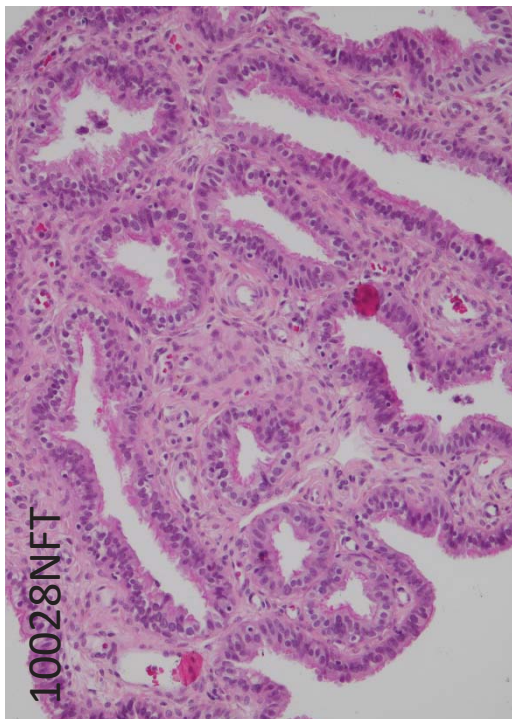
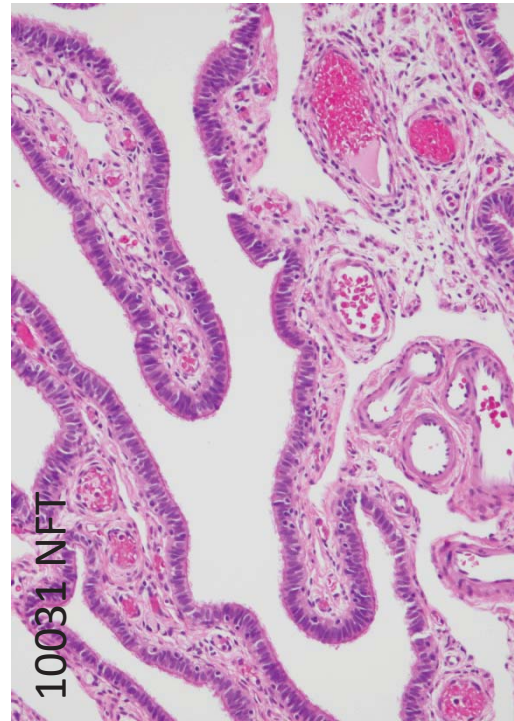
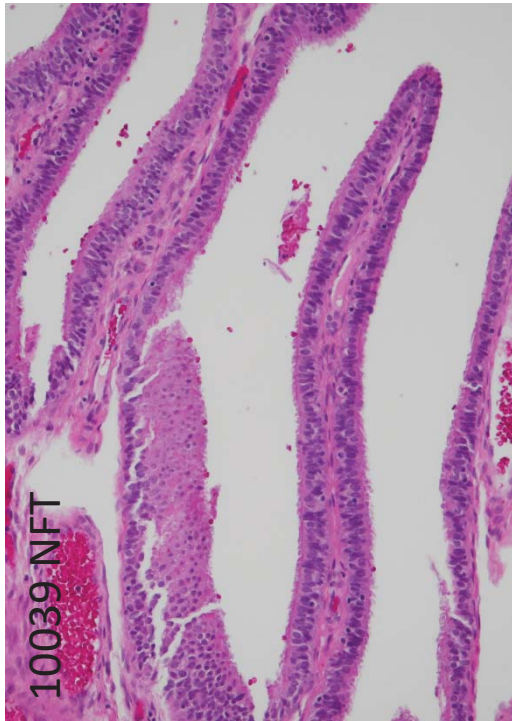
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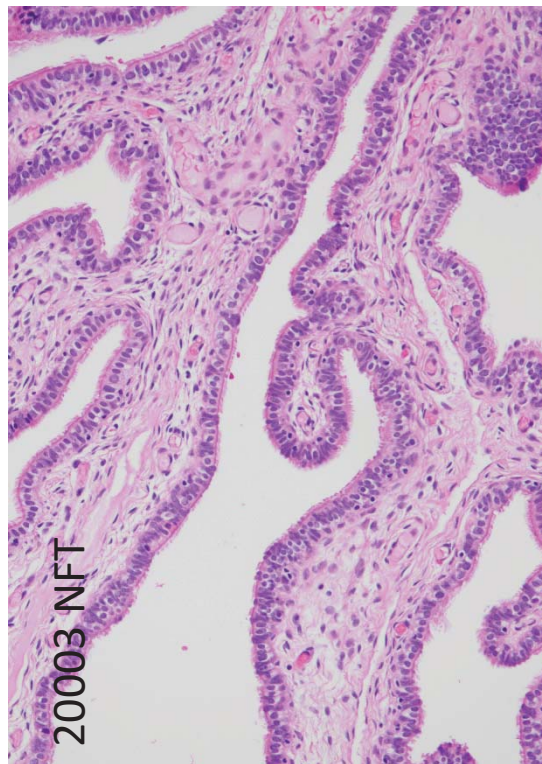
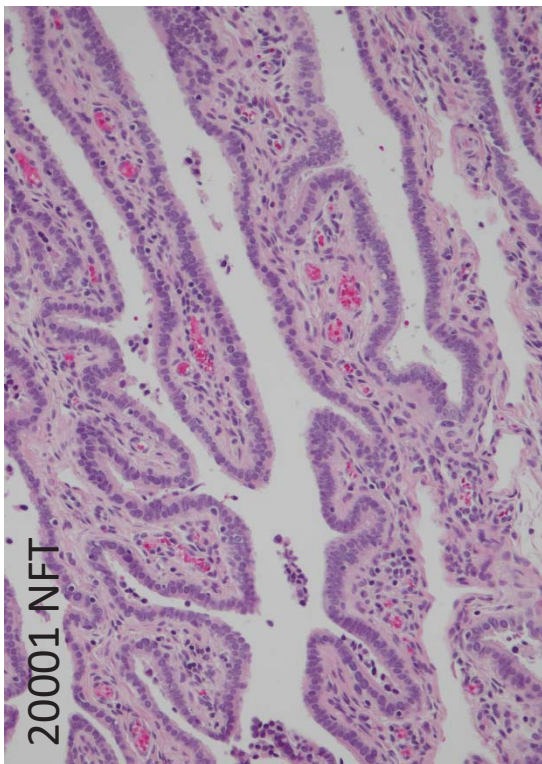
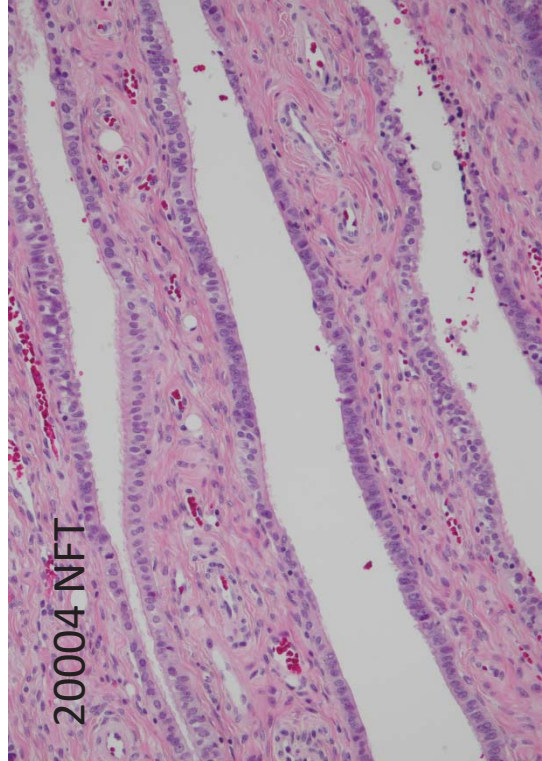
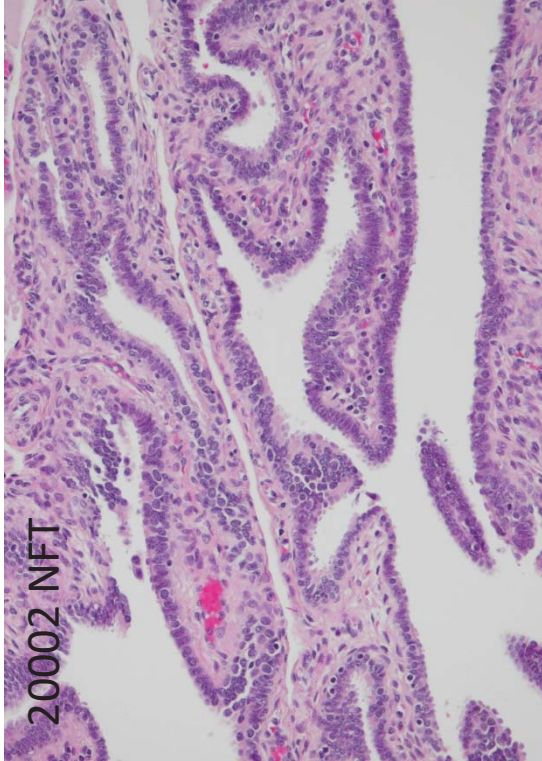


Exhibit G

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY**

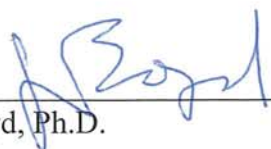
**IN RE: JOHNSON & JOHNSON TALCUM
POWDER PRODUCTS MARKETING, SALES
PRACTICES AND PRODUCTS LIABILITY
LITIGATION**

MDL NO. 16-2738 (FLW) (LHG)

THIS DOCUMENT RELATES TO ALL CASES

**EXPERT REPORT OF JEFF BOYD, PHD
FOR GENERAL CAUSATION *DAUBERT* HEARING**

Date: February 25, 2019



Jeff Boyd, Ph.D.

I. BACKGROUND AND QUALIFICATIONS

I am professor (with tenure) and chair of the Department of Human and Molecular Genetics and professor of Obstetrics and Gynecology, as well as associate dean for Basic Research and Graduate Programs at the Herbert Wertheim College of Medicine at Florida International University. I also serve as associate deputy director, Translational Research and Genomic Medicine, at the Miami Cancer Institute of Baptist Health South Florida. I am founding director of the Center for Genomic Medicine at the Miami Cancer Institute.

I received my bachelor's degree at Duke University and my master's and Ph.D. degrees in toxicology and biochemistry at North Carolina State University, and completed my postdoctoral training in environmental pathology at the Lineberger Comprehensive Cancer Center of the University of North Carolina at Chapel Hill. Following that, I served on the faculty (as a section head of Gynecologic Pathobiology) of the National Institute of Environmental Health Sciences, National Institutes of Health. I then joined the University of Pennsylvania as an associate professor, Division of Gynecologic Oncology, within the Department of Obstetrics and Gynecology, with a joint appointment in the Department of Genetics. From 1997-2006, I worked at Memorial Sloan-Kettering Cancer Center in New York City, where I was director of the Gynecology and Breast Research Laboratory in the Department of Surgery, and director of the Diagnostic Molecular Genetics Laboratory in the Department of Medicine. While there, I was promoted to full member (professor) with tenure-of-title. I left Sloan-Kettering to become vice president of Oncology and Research and director of the Anderson Cancer Institute at the Memorial University Medical Center in Savannah, GA. I also held appointments as professor in the Departments of Obstetrics and Gynecology, Surgery, Medicine, and Division of Basic Medical Sciences, as well as assistant dean for Research at the Mercer University School of Medicine - Savannah. From 2008-2015, immediately prior to taking my positions in Miami, I was a tenured professor and held the Robert C. Young, MD, Chair in Cancer Research at Fox Chase Cancer Center in Philadelphia, where I also served as Senior Vice President, Chief Scientific Officer, and Chief of the Division of Molecular Pathology. In addition, I was founding director of the Cancer Genome Institute.

My research focuses on the genetics and molecular genetics of gynecologic and breast cancers. I have been supported by more than \$25 million in grants from the National Institutes of Health or peer-reviewed NIH-equivalent grants, and have served as principal investigator for a National Cancer Institute Specialized Program of Research Excellence grant in ovarian cancer. Additional awards include Distinguished Cancer Scholar from the Georgia Cancer Coalition (2006) and the Rosalind Franklin Award for Excellence in Ovarian Cancer Research from the Ovarian Cancer National Alliance (2015). I have authored or co-authored more than 200 articles, reviews, book chapters and editorials on the molecular and genetic bases of gynecologic or breast cancers, and been invited to present more than 150 lectures on these topics throughout the world. I have served as a peer reviewer in many capacities, including as a standing member of scientific review groups of the National Institutes of Health, the Department of Defense cancer research program, and the American Cancer Society, and as an editorial board member for seven scientific and clinical journals. I have also served as an ad hoc peer reviewer for approximately 45 scientific and clinical journals. Among my many committee and board

memberships, I served as chair of the Scientific Advisory Committee for the Ovarian Cancer Research Fund (Alliance) for nine years, and am currently a member of the Board of Directors for the Society of Gynecologic Oncology. My current research interests include the histogenesis (cell of origin) of ovarian carcinoma, the comprehensive genomic characterization of ovarian cancer stem cells, and the genomic basis of diethylstilbestrol (DES)-induced carcinogenesis of the cervix and vagina of women exposed to DES in utero.

II. SCOPE OF REPORT

I was asked to opine on Dr. Ghassan Saed's expert report based on my experience as a molecular biologist and cancer researcher, and in particular, whether this research supports the biological plausibility of plaintiffs' theory that perineal talc use causes ovarian cancer. All of the opinions in this report are stated to a reasonable degree of scientific certainty. I am being compensated at the rate of \$600 per hour for my work on this matter and \$1200 per hour for deposition and other testimony.

III. BACKGROUND ON OVARIAN CANCER

Ovarian cancer is a term that embraces several closely-related malignancies. Of most relevance here is epithelial ovarian carcinoma (EOC), which comprises several histological subtypes that together account for approximately 90% of all cases of "ovarian cancer." These subtypes include serous, endometrioid, clear cell and mucinous EOCs. Although the histogenesis (cell of origin) of these cancers remains relatively poorly understood, it has been established that the pathogenesis of the distinct subtypes is not entirely overlapping. For example, a proportion of serous EOCs are now believed to arise in the fallopian tube, while some proportion of clear cell and endometrioid EOCs are believed to arise from implants of endometriosis on the ovary. It should also be noted that from a clinical perspective, carcinomas of the ovary, fallopian tube and primary peritoneal lining are generally treated identically (when matched for stage), in both surgical and medical contexts, and demonstrate a very similar clinical course. Hereafter in this report, the term "ovarian cancer" will be used as defined above.

Among the few accepted significant risk factors for ovarian cancer are rare inherited genetic mutations that affect certain genes, including *BRCA1* and *BRCA2*, which are estimated to substantially increase the lifetime risk of developing ovarian cancer to as high as 40% or 20%, respectively.¹ Additionally, through genome-wide associational studies (GWAS), certain other common genetic variants have been correlated with an increased risk of ovarian cancer, although these variants are associated with a substantially smaller lifetime relative risk of ovarian cancer.² Overall, genetic predisposition is currently believed to be associated with approximately 20% of

¹ Kuchenbaecker KB et al., *Risks of Breast, Ovarian, and Contralateral Breast Cancer for BRCA1 and BRCA2 Mutation Carriers*. JAMA (2017) 317(23):2402-16.

² Pharoah PD et al., *GWAS meta-analysis and replication identifies three new susceptibility loci for ovarian cancer*. Nat Genet. (2013) 45(4):362-70.

all ovarian cancers.³ It is very important to recognize that ovarian cancers associated with genetic predisposition as well as those (approximately 80%) that occur “sporadically” are all associated with the acquisition and accumulation of mutations affecting multiple cancer-related genes. So-called “hereditary cancers” differ only in the sense that the first rate-limiting genetic mutation is inherited, rather than acquired. In this sense, all ovarian cancers (and indeed all cancers generally) represent a genetic disease. Multiple mutations affecting multiple genes are required for a normal cell to progress to a malignant tumor cell, regardless of the tissue of origin. The causes of these “somatic” genetic mutations acquired in the organ in which a cancer ultimately develops remain largely unknown for ovarian cancer and most other cancers. Exceptions include a strong association between chronic inhalation of tobacco smoke and lung cancer, and prolonged exposure to ultraviolet-irradiation (sunlight) and skin cancer. Even for these examples, however, it is important to note that never-smokers develop lung cancer and that individuals with very low lifetime exposures to sunlight develop melanoma. Possible mutagenic mechanisms in ovarian and other cancer types include unknown environmental exposures and pure chance. Indeed, one prominent cancer molecular geneticist recently posited that most cancer cases may simply be attributable to bad luck – genetic mutations resulting from chance errors in the ordinary replication of the cellular genome (3.3 billion base pairs per cell) whenever one cell divides into two.⁴ If such mutations occur in certain critical genes that affect elements of the cancer cell phenotype, then tumorigenesis may ensue.

The limitations on our understanding of the causes and prevention of ovarian cancer persist notwithstanding decades of intense research efforts in this field. Underscoring these difficulties, a randomized controlled clinical trial involving more than 200,000 apparently well women attempted to assess the viability of ovarian cancer screening over the course of more than a decade. The trial was recently concluded, but shed little light on potential paths forward in identifying ovarian cancer in its earliest and potentially curable stages. As the authors summarized in the published results of this clinical trial, “[f]indings from this trial suggest that for 641 women screened annually using the multimodal strategy for 14 years, one ovarian cancer death is prevented.”⁵ This disappointing result characterizes the challenges that remain in the area of ovarian cancer research, especially in the areas of etiology and prevention.

IV. PLAINTIFFS’ EXPERTS HAVE NOT SHOWN THAT THEIR PROPOSED MECHANISMS FOR OVARIAN CARCINOGENESIS ARE PLAUSIBLE

Plaintiffs’ experts propose that talc causes inflammation, which leads to cancer, or that inflammation causes oxidative stress, which damages DNA, which results in cancer. These

³ Walsh T et al., *Mutations in 12 genes for inherited ovarian, fallopian tube, and peritoneal carcinoma identified by massively parallel sequencing*. Proc Natl Acad Sci USA (2011) 108(44):18032-7; Norquist BM et al., *Inherited mutations in women with ovarian carcinoma*. JAMA Oncol. (2016) 2(4):482-90.

⁴ Tomasetti C & Vogelstein B, *Variation in cancer risk among tissues can be explained by the number of stem cell divisions*. Science (2015) 347:78-81.

⁵ Jacobs I et al., *Ovarian cancer screening and mortality in the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS): a randomized controlled trial*. Lancet (2016) 387:945-56.

explanations are simplistic, speculative and lack sufficient scientific support to be deemed plausible. All suffer from the same flaw to various degrees: they depend on large leaps of faith connecting one process to another. My focus, however, is on Dr. Saed's report and the underlying study he conducted, which purportedly found that talc causes an oxidative stress response that is associated with an increased ovarian cancer risk.

As set forth below, Dr. Saed's report layers speculation upon speculation. The gap between his research (which is itself filled with many methodological flaws, described below) and elucidating the origins of ovarian cancer is very large. At most, if his research had been conducted in a reliable manner, it would show that placing relatively large amounts of talc on cell lines *in vitro* can alter the expression of certain genes, change the rates of cell proliferation and apoptosis, and increase the secretion of CA-125. But these observations have no bearing on whether ordinary use of talc in a woman's underwear (or perineal area) can cause ovarian cancer, which remains a speculative theory for which plaintiffs have offered no rational scientific support.

A. Study Design Issues

Use of DMSO as Solvent: Dr. Saed determined that he needed to apply talc through a liquid medium to the cells he wished to treat. But talc is poorly soluble in water, so he apparently chose DMSO (dimethyl sulfoxide), a "universal" solvent, in which to dissolve the talc. Dr. Saed apparently believed that he was controlling for the effects of DMSO by treating a control group of cells with the same solvent (but without talc dissolved in it).⁶ But he apparently paid no heed to recent research that has called into question whether the use of DMSO as a solvent can alter the effect of the treatment and skew the results.⁷ In other words, while a DMSO-only control can theoretically control for the effects of DMSO by itself, it cannot control for the possibility of an interaction between DMSO and talc or DMSO and the cells that could, in and of itself, alter the effect that talc would otherwise have on the cells (if any). Dr. Saed's failure to evaluate this possibility renders most of his results (those involving exposure of cells to talc) unreliable.

Determination of Talc Dosage: Dr. Saed used a very highly concentrated talc solution – 500 mg of talc per 10 ml of DMSO.⁸ He then applied relatively enormous doses of talc – from 5 to 100 µg/ml – directly to the treated cells.⁹ This represents a far greater talc exposure than human ovarian cells would ever be subjected to under normal physiologic conditions – including as a result of regular perineal use of talcum powder. Indeed, the evidence that *any* talc can reach the ovaries from external perineal use is weak.¹⁰ Dr. Saed never estimated the amount of talc he

⁶ Saed Dep. Vol. I 117:4-119:10.

⁷ See Hall MD et al., *Say no to DMSO: Dimethyl sulfoxide inactivates cisplatin, carboplatin and other platinum complexes*. Cancer Res. (2014) 74(14):3913-22.

⁸ Saed Rep. at 14.

⁹ *Id.*

¹⁰ International Agency for Research on Cancer, *Monographs on the Evaluation of Carcinogenic Risks to Humans* Vol. 93: Carbon Black, Titanium Dioxide, and Talc 411 (2010) ("[T]he evidence for retrograde transportation of talc to the ovaries of normal women is weak" and animal studies "showed no evidence of retrograde transport
(cont'd)

believes would reach the ovary or the fallopian tubes as a result of perineal dusting, despite being directly asked,¹¹ and other aspects of his deposition testimony support the conclusion that such an anatomical journey would prove improbable for talc particles. In attempting to explain why talc would not produce inflammation and cancer in the intervening areas of the female reproductive anatomy, for example, Dr. Saed repeatedly referred to the “wash” of bodily fluids that would expel particulate matter.¹² Dr. Saed contrasted this protective mechanism to that of the ovaries, which he claims have no mechanism for removing foreign particles.¹³ But the logical conclusion of this argument would be that the same mechanisms of expulsion of talc from areas of the female reproductive tract distal to the ovaries (vagina, cervix, uterus, fallopian tubes) should also prevent talc from otherwise migrating – like a salmon upstream – through this wash of bodily fluids, eventually reaching the ovaries.

Even accepting that talc could reach the ovaries to some extent, however, I am aware of no research suggesting that an amount approaching the quantities involved in Dr. Saed’s study would ever reach the fallopian tubes or ovaries, and Dr. Saed appears to admit as much.¹⁴ As such, Dr. Saed failed to show that the dose range he used in his studies is applicable to human exposure levels and any subsequent physiological sequela.

Moreover, Dr. Saed’s report does not articulate any reason for selecting such high doses, much less any reason why he believes a study using these mega-doses is likely to produce data relevant to carcinogenesis in humans. At his deposition, Dr. Saed suggested that he initially treated cells with an even larger dose of 1000 µg/ml, but found that this dose simply killed the cells, precluding the ability to measure any biological response, and that he, therefore, selected the lower, but still very high, doses reported in his report and manuscript.¹⁵ This is an inappropriate methodology for selecting an appropriate dose range for experiments designed to test the effect of a xenobiotic (foreign chemical or substance, naturally-occurring or otherwise) on cultured human cells *in vitro*, especially when the goal is to provide evidence that such an exposure is directly linked to carcinogenesis in humans.

A fundamental tenet of toxicology is that any chemical or substance, including those generally considered completely safe or inert (for example, food or beverage ingredients, or substances that humans consume or otherwise contact routinely), will almost certainly elicit a measurable biological or physiological response from cells or organisms that are exposed *in vitro* or *in vivo*,

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of talc to the ovaries”). See Henderson WJ et al., *Talc and carcinoma of the ovary and cervix*. J Obstet Gynaecol Br Commonw. (1971) 78(3):266-72 (finding no relationship between perineal talc use and ovarian talc burden); Heller DS et al., *The relationship between perineal cosmetic talc usage and ovarian talc particle burden*. Am J Obstet Gynecol. (1996) 174(5):1507-10 (same).

¹¹ Saed Dep. Vol. I 233:8-234:5.

¹² *Id.* 166:1-2.

¹³ *Id.* 165:11-166:2.

¹⁴ See *id.* 233:11-234:1.

¹⁵ *Id.* 55:3-12.

respectively, to any such xenobiotic when administered at an extremely high, i.e., non-physiologic, dose. That said, such biologic responses, e.g., changes in gene expression or cell proliferation, may not necessarily be associated with a “toxic” outcome, e.g., cell death or neoplastic transformation. If one is testing the hypothesis that exposure to a specific xenobiotic is plausibly linked to carcinogenesis in humans, especially if the model system is human cells cultured *in vitro*, it is only logical that the appropriate experimental design would employ a dose range compatible with an equivalent physiologic exposure *in vivo*, if the intent is to argue that the biological responses seen *in vitro* are somehow related to the carcinogenic process *in vivo*. Since it is impossible to know what level of talc, if any, may actually reach the fallopian tubes and ovaries of a woman exposed to hygienic doses of talc applied in the perineal region, the only recourse an experimentalist has in the design of such a study is to employ as large a dose range as necessary in order to elicit measurable biological perturbations. This describes, in essence, an experimental approach of convenience.

It should now be self-evident that this entire experimental design is fundamentally flawed in several respects, in terms of linking the results of these experiments to talc-induced human ovarian carcinogenesis. First and foremost, lower doses more compatible with a physiologic exposure to talc in the human female reproductive tract were not used in these experiments, even if it were possible to determine what significantly lower dose range that may be. Second, the biological perturbations observed in cultured cells exposed to high doses of talc cannot be reliably extrapolated to such biological responses *in vivo*, which is why animals (typically mice or rats) are used in studies designed to predict the human carcinogenic potential of one or another xenobiotic. Finally, absent the malignant transformation of human cells cultured *in vitro* (utilizing several assays traditionally employed to approximate malignant transformation in this context) following exposure to high doses of talc, the rather non-specific biological responses observed in Dr. Saed’s experiments cannot be interpreted to conclude that talc exposure causes ovarian cancer *in vivo*. At most, the only conclusion that may be reasonably made from these experiments is that exposure to extremely high doses of talc results in the biological perturbation of human cells cultured *in vitro*,¹⁶ a result that is entirely expected based on well-established principles of toxicology. Several of the problematic experimental issues discussed above will be expanded upon below.

Inadequate Control Experiments: Dr. Saed’s studies do not adequately address his hypothesis that there is a biological mechanism linking exposure to talc (a hydrated magnesium silicate compound consisting of magnesium, silicon and oxygen – all of which are found at one or another concentration in the human body, and are in fact considered “essential elements”) to ovarian carcinogenesis because Dr. Saed failed to perform additional control experiments designed to test whether other particulate compounds, such as, for example, cornstarch (a powdered carbohydrate derived from the endosperm of corn kernels) or a particulate compound more chemically similar to talc, such as finely ground beach sand (silicon dioxide) produced the same results. Such experiments testing the potential biological effects of other particulate compounds like talc could have been used to determine whether his findings were driven by

¹⁶ Saed Rep. at 14.

some quality that is unique to talc, or rather its particulate form generally, the characteristics of which are shared by many other compounds.

Specifically, in his investigation, talc was dissolved in DMSO and added to cultured cells as an experimental condition.¹⁷ Changes in the levels of RNA and protein expression in these cells were then measured by qPCR (quantitative polymerase chain reaction) and ELISA (enzyme-linked immunosorbent assay) techniques and compared with levels found in cells treated with DMSO only.¹⁸ Dr. Saed concluded that differences in RNA and protein expression between the talc-treated and DMSO-only-treated samples were evidence of an “oxidative stress” response induced by talc exposure.¹⁹ Overlooked, however, was the possibility that these differences were the result of high-dose particulate exposure generally, and not to talc exposure specifically.

A properly designed experiment would have included a condition(s) where cultured cells were treated with at least one, and preferably several, additional non-talc compounds suspended in DMSO. Such control experiments would help an investigator discern the baseline RNA and protein expression level changes that occur in response to addition of particulate matter generally to cultured cells. Dr. Saed testified that the inclusion of such a condition would have been feasible.²⁰ He admitted that he did not know whether the addition of an inert substance, such as corn starch, to the cell cultures would have yielded the same RNA and protein expression changes that he observed in talc-treated cell cultures.²¹ When confronted with the issue of exclusion of such control experiments, Dr. Saed erroneously concluded that inert substances could not cause a similar oxidative stress response profile because the “untreated” cells exposed to DMSO only “didn’t show that.”²² The manner in which cultured cells respond to the addition of DMSO alone has no bearing on how they may respond to the addition of DMSO containing a suspended inert particulate substance other than talc.

The failure to include such control experiments to measure potential “oxidative stress responses” to inert particulate substances is a fatal flaw with respect to the veracity of the investigative power of the aforementioned studies to establish a cause and effect relationship between talc exposure and a cellular oxidative stress response. Dr. Saed’s only defense to this fundamentally flawed experimental design was that he “tested several fold.”²³ However, repeating the same flawed experiment several times cannot overcome this underlying methodological flaw.

Dr. Saed’s experiments neither contradict nor support his hypothesis that there is a biological mechanism(s) through which talc may induce an oxidative stress response in cultured human

¹⁷ Saed Dep. Vol. I 273:10-14.

¹⁸ Saed Rep. at 14-15.

¹⁹ *Id.* at 14-18.

²⁰ Saed Dep. Vol. I 274:5-9.

²¹ *Id.* 273:16-25.

²² *Id.* 272:20-273:2.

²³ *Id.* 272:14-19.

cells. He merely showed that there are changes in the expression levels of specific RNA and protein molecules that differ between cells treated with DMSO and cells treated with DMSO containing talc. As such, Dr. Saed's studies offer no support for his opinion regarding the biological mechanism by which talc allegedly causes an oxidative stress response in cultured cells *in vitro*, and much further, ovarian carcinogenesis *in vivo*.

Cell lines: There are serious methodological concerns with respect to the types of human cells that were used in Dr. Saed's experiments. Four distinct categories of primary cells or established cell lines were used: 1) The EL1 cell line, derived from human spleen and classified as a monocyte/macrophage cell type; 2) "Normal ovarian epithelial" cells – it may be inferred from Dr. Saed's laboratory notebook and the commercial source of these cells (Cell Biologics) that they are "human primary ovarian epithelial cells derived from normal human ovary tissue"; 3) The FT33 cell line, described by the commercial source as "immortalized human fallopian tube epithelial cells"; and 4) Three human ovarian carcinoma cell lines, SK-OV-3, A2780, and TOV-112D, which are, by definition, derived from human ovarian carcinomas.²⁴ All three of the ovarian carcinoma cell lines are originally from the American Type Culture Collection; the latter two are described as having been derived from endometrioid ovarian adenocarcinomas, and the SK-OV-3 cell line was derived from ovarian carcinoma ascites (histologic subtype unknown).²⁵

It is not at all clear why one would conduct experiments related to xenobiotic-induced ovarian carcinogenesis using a cell line (EL1) derived from the monocyte/macrophage lineage, a white blood cell type involved in the adaptive immunity process. It is similarly unclear why one would conduct such experiments using human ovarian carcinoma cell lines (SK-OV-3, A2780, and TOV-112D); if an experimentalist is testing the hypothesis that exposure of human ovarian cells to a potential carcinogen leads to biological effects related to the tumorigenic process, why would cell lines that are derived from ovarian carcinomas represent an appropriate model? These cells, *ipso facto*, represent the ultimate culmination of the tumorigenic process, and would be expected to possess myriad biological and somatic genetic differences compared to "normal" ovarian epithelial cells. Stated simply, the approach of testing a hypothesis as to how cancer may be experimentally induced, *using cancer cells*, is seriously unsound.

B. Misinterpretation of Results

CA-125 Findings: Dr. Saed reports an increase in cellular release of the CA-125 protein following talc treatment and claims that this "highlight[s] the implications of the pro-oxidant states caused by talc. . . ."²⁶ This is a confusing assertion because Dr. Saed does not identify the "implications" that increased CA-125 expression purportedly "highlight[s]." If he intends to suggest that increased CA-125 secretion is suggestive of ovarian carcinogenesis, however, then he misunderstands the clinical use of serum CA-125 protein measurements.²⁷ The FDA-

²⁴ Saed Dep. Vol. I, Ex. 1 at SAED000001 (Expert Report Notebook Files).

²⁵ *Id.*

²⁶ Saed Rep. at 18.

²⁷ Notably, in his deposition, Dr. Saed admitted that that he does not know the clinical significance of CA-125. Saed Dep. Vol. I 248:25-250:2.

approved use of measuring serum CA-125 levels is in the context of a “biomarker” to monitor response to ovarian cancer treatment.²⁸ Although such measurements have also been tested experimentally for decades in an effort to detect ovarian cancer at an early stage, the specificity and sensitivity of serum CA-125 levels in this context are unacceptably low, and the assay is neither useful nor approved for this purpose.²⁹ Increased serum CA-125 levels have been reported in “benign conditions such as endometriosis, pregnancy, ovulatory cycles, liver diseases and congestive heart failure, as well as in infectious disease such as tuberculosis.”³⁰ Serum levels of CA-125 are also elevated in non-ovarian cancers, such as “breast cancer, mesothelioma, non-Hodgkin lymphoma, gastric cancer, and leiomyoma and leiomyosarcoma of gastrointestinal origin.”³¹ Therefore, any increase in CA-125 levels observed by Dr. Saed is not necessarily indicative of malignant conditions, much less malignant risk. Because increased CA-125 expression can reflect any number of causes, physiologic states, or conditions other than ovarian cancer, its use as a detection tool is highly disfavored and is considered ineffective from a clinical perspective. Nor does it play any role in ovarian cancer causation. Therefore, any effect that exposure to talc may have on cellular release of CA-125 is irrelevant to the question whether it plays any role in causing ovarian cancer.

Some of the utility of CA-125 as a biomarker does stem from the fact that CA-125 secretion can increase with the onset of ovarian cancer. As discussed, however, CA-125 secretion is highly non-specific and increases are more frequently unrelated to ovarian cancer. Furthermore, clinical use of CA-125 as an early detection marker for ovarian cancer is typically accompanied by a transvaginal sonography.³² Even then, “reports suggest that sensitivity of early stage disease is limited.”³³ If CA-125 is not even a reliable biomarker for the *onset* of ovarian cancer *in vivo*, it is doubtful that CA-125 can be a reliable biomarker for the *increased risk* of onset of ovarian cancer *in vitro*. To the extent that an increase in CA-125 secretion is sometimes associated with ovarian cancer, Dr. Saed still has not shown that CA-125 is a cancer precursor, rather than an effect of such cancer.

These opinions are generally shared by Reviewer #1, who provided a critique of Dr. Saed’s manuscript following submission to *Gynecologic Oncology*. The Reviewer writes that, “The significance of this study would be greatly enhanced if a mouse model corroborated the cell line findings. In this reviewer’s opinion, the cell line studies alone and the increase in CA-125 while intriguing are not sufficiently convincing.”³⁴

²⁸ Saed Rep. at 18 (citing Jelovac D & Armstrong DK, *Recent progress in the diagnosis and treatment of ovarian cancer*. CA Cancer J Clin. (2011) 61(3):183-203).

²⁹ See above reference to UKCTOCS clinical trial.

³⁰ Scholler N & Urban N, *CA125 in Ovarian Cancer*. Biomark Med. (2007) 1(4): 513-523 (internal refs. omitted).

³¹ *Id.* at 517 (internal refs. omitted).

³² *Id.*

³³ *Id.*

³⁴ Saed Dep. Vol. II, Ex. 35 at 2, Gynecologic Oncology Email dated Sept. 19, 2018 re: GYN-18-1020: Final Decision (“Gynecologic Oncology Decision”).

Finally, the conclusion stated in the Abstract and elsewhere in the manuscript by Fletcher *et al.* (rejected by *Gynecology Oncology* and under review or perhaps in press at *Reproductive Sciences*), stating that, “Talc exposure also resulted in a significant increase in inflammation as determined by increased tumor marker CA-125,” is incorrect and misleading.³⁵ There was no direct measurement of inflammation in the cultured cells, and a correlation of increased CA-125 secretion with inflammation is speculative at best.

Cell Proliferation and Apoptosis Findings: Dr. Saed claims that he has “shown conclusively that talcum powder . . . enhance[s] cell proliferation, and inhibit[s] apoptosis in EOC cells,” as well as in “normal cells, including surface ovarian epithelium, fallopian tube, and macrophages.”³⁶ At his deposition, he took this claim further, asserting that cell proliferation “is an indirect measure of the beginning of [neoplastic] transformation.”³⁷ None of this is correct, and Dr. Saed’s attempt to equate cell proliferation with cancer development is profoundly unscientific. As noted above, the lack of appropriate control experiments undermines the specificity of his findings to talc powder, making it impossible to issue such a “conclusive[]” claim. In fact, cell proliferation is a natural response to stress, meaning that this result would be expected to follow many cell treatments *in vitro* and would not remotely be unique to exposure to large doses of talc suspended in DMSO.

In addition, it is unclear why these findings are significant since Dr. Saed testified that there are no studies showing that increased cell proliferation and decreased apoptosis are associated with ovarian cancer risk.³⁸ The findings also seem irrelevant because Dr. Saed was not aware of any studies showing that these cellular responses are present in any tissue in women who use talc.³⁹ Nor am I. Regardless, Dr. Saed’s broad characterization of these properties as an “oncogenic phenotype”⁴⁰ is not consistent with scientific knowledge.

First, cell proliferation is a regular process in tissue homeostasis, and does not indicate that a normal cell has transformed into a cancer cell. Dr. Saed acknowledged this when he explained that “temporary or initial induction of proliferation [] is a normal response of all normal cells to agents.”⁴¹ Dr. Saed does not explain in his report why his findings are not simply a typical cellular response to the introduction of a foreign agent, such as talc, in cell culture. Furthermore, according to his lab notebooks, the furthest data collection time point in Dr. Saed’s investigation was 72 hours after treatment with talc. At best, Dr. Saed’s study provides a snapshot of the

³⁵ Saed Dep. Vol. I, Ex. 7 & 8 at 2 (Fletcher NM, Harper AK, Memaj I, Fan R, Morris RT, Saed GM, *Molecular basis supporting the association of talcum powder use with increased risk of ovarian cancer* (2019) (unpublished manuscript)) (“Manuscript”) at 2.

³⁶ Saed Rep. at 16.

³⁷ Saed Dep. Vol. II 464:2-11.

³⁸ Saed Dep. Vol. I 268:4-269:4.

³⁹ *Id.* 268:25-269:4.

⁴⁰ Saed Rep. at 17.

⁴¹ Saed Dep. Vol. I 265:10-15.

initial reaction of cells to particulate exposure. It is unreasonable to extrapolate from these findings that cells are therefore “oncogenic” and any observed fluctuations in proliferation and apoptosis are permanent. Dr. Saed’s findings on proliferation and apoptosis do not seem to have any bearing on whether talc increases the risk of ovarian cancer.

C. Limitations of Results and the Need for Further Study

Alterations in Expression Levels and Activities of the Enzymes Studied Do Not Equate to an Altered State of Oxidative Stress in the Cultured Cells: As described in much of the evidence submitted by Dr. Saed in the context of expert testimony, including laboratory notebooks, the transcript of his deposition, and perhaps most succinctly, the manuscript by Fletcher *et al.* summarizing his findings, he consistently states and otherwise implies, many times, that decreased expression and activity of the antioxidant enzymes CAT and SOD3, increased expression and activity of the pro-oxidants iNOS, NO₂-/NO₃-, and MPO, and decreased expression and activity of antioxidant enzymes GSR and GPX “enhances the pro-oxidant state in . . . cells.”⁴² While he reports RNA levels (“expression”) of these enzymes, as measured by qPCR, that are altered (up or down) following exposure to talc for 72 hours, he frequently conflates “expression and activity” of these enzymes as assessed by an ELISA, which measures protein levels.⁴³ The reactions that these enzymes catalyze may alter the levels of reactive oxygen species (typically nitrogen- or oxygen-based), but these reactive oxygen species are very unstable and cannot be measured by an ELISA. As best as I can tell from his laboratory notebooks, and from the content of the manuscript, he is using protein levels, as measured by an ELISA, to estimate the amount of enzymatic activity that a certain quantity of protein may have. This is an indirect and misleading presentation of the data. *Regardless*, none of these data are indicative of an increased pro-oxidant state in the cultured cells *in vitro*, much less *in vivo*.

The Single Nucleotide Polymorphism (SNP) Findings are Vague and of Questionable Relevance: *First*, Dr. Saed has not established that his findings actually represent mutations, as he claims in his manuscript. In Table 2, he lists what he believes to be talc-induced genetic mutations resulting in SNP genotype switches in “key redox enzymes.”⁴⁴ But as he acknowledged at his deposition, he was not “able to estimate the volume of cells that this genotype switch occurred in.”⁴⁵ Rather, his technique only reports whether there is a “population of cells that acquired th[e] genotype” at issue.⁴⁶ This limitation is significant because it cannot rule out the possibility that the cells under treatment had one of three possible SNP genotypes (heterozygous, homozygous for minor allele, or homozygous for major allele) already, prior to treatment – in other words, that Dr. Saed was not finding treatment-induced mutations at all, but

⁴² Manuscript at 2.

⁴³ *Id.* at 20-22 (panels A and B of each figure show RNA expression, while panels C and D of each figure show protein levels as measured by ELISA).

⁴⁴ *Id.* at 19 (Table 2).

⁴⁵ Saed Dep. Vol. I 198:13-199:15.

⁴⁶ *Id.*

rather preexisting genetic variability that became manifest after the expansion of one or another subpopulation of cells in culture as a result of variable proliferation of a heterogeneous cell population. Indeed, the term “single nucleotide polymorphism” is by definition a type of genetic variation that exists in a population at a particular nucleotide position in a particular gene. In other words, polymorphisms represent naturally occurring genetic variants, not “mutations”, at least in the context of putative carcinogen-induced mutagenesis over a 72-hour period. This occurs when a specific nucleotide in a specific gene is variable throughout a population, occurring when one genetic variant is inherited from one parent and the other genetic variant is inherited from the other parent. At a typical SNP site in the human genome, an individual may be homozygous for the SNP (for example T/T or C/C), or heterozygous for the SNP (C/T). These are not mutations. They represent the genetic basis of human phenotypic variation, and one may find SNPs in the great majority of human genes. This well-established genetic phenomenon throws Saed’s entire claim of talc-induced mutations into doubt.

Second, none of the SNPs identified by Dr. Saed in his background discussion of ovarian cancer-associated polymorphisms was observed in his talc study. Dr. Saed broadly states in his report that SNPs in genes that code for certain enzymes (such as *CAT*, *GPX1*, *GSR* and *SOD2*) have been associated with increased ovarian cancer risk.⁴⁷ In making this statement, Dr. Saed relies, in part, on the Belotte study, conducted in his lab, which actually found an association between a specific SNP in the *CAT* gene and ovarian cancer **survival**, not risk. Dr. Saed fails to elaborate on his statement and only identifies three SNPs in redox genes that he claims are related to ovarian cancer risk: rs1001179 (reducing *CAT* activity), rs4673 (reducing *CYBA* activity) and rs2333227 (occurring in the *MPO* gene).⁴⁸ The rs1001179 polymorphism is actually associated with ovarian cancer survival, not risk.⁴⁹ And a meta-analysis of 43 case-control studies involving various types of cancer found no association between the rs2333227 polymorphism (*MPO*) and an increased cancer risk.⁵⁰ Regardless, none of the underlying studies referenced by Dr. Saed is a genome-wide association study (GWAS) that examined the prevalence of a given SNP in a larger population of ovarian cancer patients. In other words, even if these three SNPs were hypothesized to be associated with ovarian cancer risk in isolated, statistically-underpowered investigations, their significance when it comes to the broader questions of ovarian cancer risk in the general population has not been established.

Perhaps recognizing this gap in his analysis, Dr. Saed also lists a number of additional SNPs identified by GWAS that influence ovarian cancer risk.⁵¹ It is unclear whether these polymorphic variants are associated with an increased or decreased risk. None of the variants

⁴⁷ Saed Rep. at 7-8.

⁴⁸ *Id.* at 8.

⁴⁹ Belotte J et al., *A single nucleotide polymorphism in catalase is strongly associated with ovarian cancer survival*. PLoS One. (2015) 24:10(8):e0135739.

⁵⁰ Chu H et al., *The MPO –463G>A polymorphism and cancer risk: a meta-analysis based on 43 case-control studies*. Mutagenesis. (2010) 25(4):389-95.

⁵¹ Saed Rep. at 8.

seem to occur in protein-coding regions except possibly rs2072590, which is “located at 2q31” within “a family of *HOX* genes.”⁵² The remaining variants occur “near” *BNC2* and *MERIT40*, “downstream” of *MYC*, and “intronic” to *SKAP1* and *TIPARP*.⁵³ At most, these SNPs could theoretically function to regulate the expression of genes, but not functions of the encoded protein, if they have any effect at all. It is certainly far from evident that any of these genes is involved in the redox state of cells.

Third, none of the “mutations” that Dr. Saed observed in his talc-treated cells has been reported by GWAS to be associated with an increased ovarian cancer risk. It should be noted that many SNPs are “silent,” in that they do not result in any change in activity by the protein, and Dr. Saed has failed to show that the SNPs he claims resulted from talc-induced genotype switching are related to altered functions of the genes under study. Dr. Saed lists *CAT* (rs769217), *NOS2* (rs2297518), *GSR* (rs2448), *GPX1* (rs2448) and *SOD3* (rs2536512) genetic variations in Table 2 of his manuscript.⁵⁴ He was unable to state whether these SNPs have been reported to occur in women using talc.⁵⁵ And as discussed below, the observed “mutations” in *CAT*, *NOS2*, and *GPX1* fail to support his conclusions, for a number of additional reasons. Notably, the *GSR* and *SOD3* genes were not affected at all by talc treatment, as reported in Table 2.

CAT (rs769217) SNP. Dr. Saed did not observe this “mutation” in A2780 and SK-OV-3 cell lines. If this mutation is the mechanism by which talc allegedly increases ovarian cancer risk, it is unclear why the mutation is not commonly seen across all talc-treated cells. Dr. Saed makes many logical leaps to connect this genetic variant to an elevated cancer risk.

First, Dr. Saed states that the SNP results in an isoleucine to threonine amino acid change, but no more information is provided as to how or whether this change affects protein function.⁵⁶ Does the mutation alter the catalytic site of the enzyme? Does it affect secondary and tertiary structures of the protein or modify its interactions with other molecules? Dr. Saed’s only observation is that talc-treated cells exhibit decreased *CAT* expression and catalase activity. However, he acknowledges in his report that these changes may be caused by other mutations in *CAT*, and not the rs769217 variant itself.⁵⁷ In fact, it would be much more logical to conclude that lower amounts of *CAT* protein in a cell would result in lower *CAT* activity (converting hydrogen peroxide to water and oxygen). Nevertheless, there are many straight-forward follow-up experiments that Dr. Saed could have conducted to understand the specific effect of the rs769217 genetic variant on catalase activity (if any). Scientists regularly create cell lines with targeted mutations through the use of genetic editing tools (such as CRISPR/Cas9), to study the impact of specific genetic mutations on protein functions. Dr. Saed could have repeated his

⁵² *Id.*

⁵³ *Id.*

⁵⁴ Manuscript at 19 (Table 2).

⁵⁵ Saed Dep. Vol. I 225:17-226:3.

⁵⁶ Manuscript at 19.

⁵⁷ Saed Rep. at 18.

ELISA assays and done pull-downs of the catalase protein in normal cells and cells with targeted mutations to understand whether and how the rs769217 mutation affected the catalase function and its interaction with other molecules (including its function as a tetramer). Only with these sorts of follow-up experiments could Dr. Saed actually attribute a causal relationship between this specific genetic variant and the protein activity observed.

The minor allelic frequency (MAF) of the rs769217 SNP was described as 12.3%.⁵⁸ As presented, this figure can only be derived from the genotypes of large numbers of individuals in a population. For a single individual, the MAF would by necessity be 0, 50%, or 100%. These are basic principles of human genetics. In the talc treatment experiments, data are presented as Allele 1 and Allele 2 scores with and without talc treatment; in the case of TOV-112D cells, for example, the C/C genotype at rs769217 becomes C/T following talc treatment with scores of Allele Amp Scores of 0.67 and 0.88.⁵⁹ Although it is not clear exactly what these scores represent (the total is greater than 1.0), it may be assumed that a substantial proportion of the cells exposed to a dose of talc for 72 hours sustained a C to T mutation. I have never witnessed such potent mutagenesis by any agent – especially within a narrow 72-hour post-treatment window. Dr. Saed was similarly unable to recall any agent that has produced such rapid, robust mutagenesis.⁶⁰ It is highly unlikely that the increased MAF is due to genotoxicity that is unique to talc, considering a previous study found that talc was not genotoxic.⁶¹ Rather, the high MAF is likely the result of general genotoxicity associated with the introduction of extremely high dosages of foreign particulate into cell cultures, the selective expansion of small numbers of cells present in culture with the MAF, otherwise undetectable, as the cells were induced to proliferate by talc exposure, some sort of experimental error, or all of the above. The inclusion of appropriate control experiments (as previously described) could have shed light on these questions. Finally, as noted elsewhere in this report, the allele frequencies for all the studied SNPs should have been presented in a quantitative fashion, rather than qualitative. For a mutation to be “fixed” in an affected cell, the cell must obviously undergo division to two daughter cells. That specific SNP sites that happened to be associated with enzyme activity of the “critical” genes under study underwent qualitative mutagenesis from one nucleotide to another in 100% of the talc-treated cells, in 72 hours, is not only implausible, it is *impossible*, in light of the doubling time of proliferating cells.

SOD3 (rs2536512) and GSR (rs8190955) mutations. Dr. Saed’s report states that these “SNP genotypes were not detected in any cell line.”⁶² Part B of Table 2 confirms that neither the control nor talc-treated cell lines had mutations at these locations.⁶³ However, the first part of

⁵⁸ Saed Dep. Vol. I, Ex. 1 at SAED000078.

⁵⁹ *Id.* at SAED000080.

⁶⁰ Saed Dep. Vol. I 252:3-7.

⁶¹ Endo-Capron S et al., *In vitro response of rat pleural mesothelial cells to talc samples in genotoxicity assays (sister chromatid exchanges and DNA repair)*. *Toxicol In Vitro*. (1993) 7(1):7-14.

⁶² Saed Rep. at 18; Manuscript at 11.

⁶³ Manuscript at 19.

the table still lists the MAF of mutations as 19.1% and 47.6%, respectively.⁶⁴ As for the CAT gene data above, it is unclear from whence the MAF data are derived. Is it a calculation of allelic frequency based on the total pooled alleles from all of the talc-treated cells? Is it an average of the MAF values calculated individually for each of the talc-treated cell lines? Is it the naturally-occurring frequency of the mutation in the general population? If it does refer to the frequency in the general population, what proportion of cells treated with talc actually displayed these mutations?

Regardless of how the MAF data were calculated, if no SNP genotypes were detected in the cell lines, how can these *SOD3* and *GSR* mutations still be attributed to changes in redox activity and provide any basis for Dr. Saed's theory that talc exposure leads to mutations associated with an increase in ovarian cancer risk?

NOS2 (rs2297518) mutation. The concerns described above also apply to the *NOS2* mutation. This mutation was not found in the talc-treated A2780 or TOV-112D cell lines, had a MAF of 17.3% and resulted in a serine to leucine amino acid change.⁶⁵ No additional studies were conducted to confirm that observed increases in protein activity were actually caused by the rs2297518 mutation.

GPXI (rs3448) mutation. In addition to the concerns described above, other issues also undermine the significance of the *GPXI* findings. First, Dr. Saed focuses on the mutation because the "acquisition of chemoresistance by ovarian cancer cells is associated with a switch from *GPXI* SNP genotype to the normal *GPXI* genotype."⁶⁶ It is unclear how any chemoresistance finding in already cancerous cells is relevant to understanding whether an association exists between talc exposure and ovarian cancer risk. Among genes coding for glutathione peroxidase enzymes, only the rs6456822 SNP in *GPX6* has been reported as having a genome-wide significance for association with serous epithelial ovarian cancer risk.⁶⁷ Simply put, Dr. Saed does not provide any basis for why the rs3448 genetic variant is associated with ovarian cancer risk.

Dr. Saed did not observe the *GPXI* conversion in one of the normal cell lines (HOSEpiC) after exposure to talc. As with the *CAT* mutation, if this mutation is the mechanism by which talc allegedly increases ovarian cancer risk, it is unclear why the mutation did not occur in all normal cells treated with talc. Showing this mutation occurs in all normal cells treated with talc would be the first step toward understanding any biological mechanism whereby talc allegedly leads to an increased risk of ovarian cancer.

⁶⁴ *Id.*

⁶⁵ *Id.*

⁶⁶ Saed Rep. at 19.

⁶⁷ Kuchenbaecker KB et al., *Identification of six new susceptibility loci for invasive epithelial ovarian cancer*. Nat Genet. (2015) 47(2):164-71.

Finally, Dr. Saed describes the amino acid changes and effect on protein activity for the *GPXI* mutation as “unknown.”⁶⁸ Dr. Saed has no idea why the mutation is significant to his opinion on talc and ovarian cancer risk other than the fact that the mutation occurs in a gene involved in redox activity. The mere existence or creation of a mutation is not necessarily biologically significant. For example, the SNP could be a synonymous mutation that does not result in any amino acid change in the resulting protein and has no consequence on glutathione peroxidase enzyme function. If the SNP did result in an amino acid change, the change could be inconsequential because it does not affect the activity of the enzyme, the secondary or tertiary structures of the protein or how the protein interacts with other molecules. As it stands, there is no basis for the relevance of the *GPXI* mutation in studying ovarian cancer risk.

My interpretation of the experimental design and presentation of data related to the measurement of SNP genotypes in several genes involved in the general oxidative state of the cell, after exposure to talc, is that Dr. Saed has conflated mutagenesis with normal genetic variation, especially as the latter may exist in a highly heterogeneous state in cells cultured *in vitro*. It is not at all clear how these data bear on the purported risk of talc for the development of ovarian cancer. This view would seem to be shared by Reviewer #1 of the manuscript submitted to *Gynecologic Oncology*, who writes, “The significance of SNP alterations should be further clarified.”⁶⁹

If Dr. Saed had been interested in demonstrating that talc was indeed mutagenic (creating mutations) in his cell lines, the most appropriate experiments would have examined global mutagenesis in a much broader context. One potential experiment would involve comparing talc-treated cells to untreated cells with respect to potential mutations generated throughout the entire exome (coding region of the genome). This experiment would have involved extraction of DNA from treated vs. untreated cells, followed by sequencing of the entire exomes of these cells using next-generation DNA sequencing technology. This technology is typically available in core facilities of most research universities and academic medical/cancer centers, and if not, is readily performed by myriad commercial laboratories for a modest cost. An alternative approach would have been to perform next-generation DNA sequencing analysis of a panel of several hundred genes known to be involved (“driver genes”) in carcinogenesis when mutated. Such analyses are also performed by many commercial laboratories.

In summarizing my conclusions on scientific clarity and relevance of the SNP studies, I can only conclude that the rationale of studying talc-induced mutagenesis occurring *exclusively* at SNP sites in some of the genes encoding enzymes under study, including the anti-oxidant enzymes CAT, GSR, GPX1, and SOD3, and the pro-oxidant enzyme NOS2, appears to represent a chain of logic by Dr. Saed that would correlate talc-induced mutations at these specific sites with altered enzymatic activity of the encoded proteins, followed by increased oxidative stress in the affected cells; this complex theoretical sequence of talc-induced events in cultured cells would appear to tie all of his various hypotheses together. Parenthetically, there is no evidence or

⁶⁸ Manuscript at 19.

⁶⁹ Gynecologic Oncology Decision at 2.

suggestion provided in Dr. Saed's manuscript as to how the enzymes affected by talc exposure (expression levels) were so affected if they ***did not contain SNPs subject to mutagenesis*** and thus not studied at all (*MPO*), or ***did*** contain SNPs of purported functional consequence but ***did not sustain mutagenesis by talc*** (*GSR* and *SOD3*). These data are presented in Table 2 of Dr. Saed's manuscript. In my expert opinion, this experimental design and interpretation of results are deeply flawed, naïve, and the results regarding qualitative (as opposed to quantitative) mutagenesis at specific SNP sites are, candidly, very difficult to believe. I have expanded upon all the critical elements of this paragraph elsewhere throughout this Expert Report.

Limitations of Studies *in vitro*: Even if Dr. Saed's research methodology were flawless, and his conclusions unassailable, his studies *in vitro* would not establish a mechanism of carcinogenesis *in vivo*. The most even Dr. Saed claims to have actually shown with his experiment is a change in the levels of RNAs and proteins that encode certain proteins, changes in the activities of some of these proteins (by inference), an increase in cell proliferation and a decrease in apoptosis in response to talc exposure; but there is an enormous gap between such findings in a petri dish and proving that a particular agent is actually a probable cause of ovarian cancer.

Indeed, as a general rule, a study *in vitro* cannot, by itself, support conclusions about anything that happens in actual animal or human tissues. At most, careful studies *in vitro* may generate hypotheses that may be tested with follow-up studies using models *in vivo*, e.g., animals. The comments on Dr. Saed's manuscript reflect this principle. According to Dr. Saed's deposition testimony, *Gynecologic Oncology*⁷⁰ declined to publish his paper, and a reviewer explained that he "needed to do *in vivo* . . . animal experiments."⁷¹ I note, too, that Dr. Saed volunteered at his own deposition that, in order to determine whether his experiments truly emulated chronic inflammation in humans, he would "have to do animal studies."⁷²

The need for studies *in vivo* to evaluate Dr. Saed's results *in vitro* is especially glaring here, because previous work *in vivo* on the relationship between talc and ovarian cancer tends to refute, rather than support, Dr. Saed's conclusions. I am not aware of any research *in vivo* specifically addressing the effects of talcum powder exposure on oxidant and anti-oxidant enzymes and resultant oxidative stress in human cells. Two animal studies, however, have shown no increase in ovarian cancer development following talcum powder treatment. Hamilton, *et al.*, injected rats with mega-doses of talc adjacent to the ovaries, and reported no inflammation or neoplasia.⁷³ Keskin, *et al.*, exposed rats to talc either intra-vaginally or on the perineum. While certain infections developed (likely because the talc was not sterile), there was

⁷⁰ Dr. Saed testified that he submitted his manuscript to a journal called "*OB-GYN Oncology*." I am aware of no journal with that name, and subsequent document productions from Dr. Saed make clear that he intended to refer to *Gynecologic Oncology*.

⁷¹ Saed Dep. Vol. I 46:22-47:2; *see also* Gynecologic Oncology Decision.

⁷² Saed Dep. Vol. II 542:16-25.

⁷³ Hamilton TC et al., *Effects of talc on the rat ovary*. Br J Exp Pathol. (1984) 65(1):101-6.

no neoplastic change in any of the exposed animals.⁷⁴ Dr. Saed is capable of performing studies *in vivo* to challenge these conclusions, but said at his deposition that he lacks the time and the money for it.⁷⁵ In light of the data from earlier studies, I am skeptical that Dr. Saed's findings could be replicated *in vivo*, and without such replication, they are insufficient to reliably suggest the carcinogenic mechanism that he proposes.

Relatedly, Dr. Saed is presupposing that talc can travel to the fallopian tubes or ovaries and cause inflammation there, but his *in vitro* experiments obviously cannot evaluate that assumption, and support from existing research is lacking. In fact, Dr. Saed's suggestion that it is widely accepted that talc applied to a woman's underwear will travel to her ovaries against gravity⁷⁶ and that studies of sperm are somehow relevant to this question⁷⁷ ignores fundamental anatomy. Notably, the often-cited study regarding the presence of talc in ovarian tissue of women with ovarian cancer discovered talc both in women who reported perineal talc use and women who did not, suggesting that the talc came from a different source.⁷⁸

With respect to Dr. Saed's assertion that his data support a role for oxidative stress (presumably produced by talc exposure) in ovarian carcinogenesis, in addition to my concerns raised in this report, both Reviewers for *Gynecologic Oncology* commented on this assertion specifically as it was articulated in Dr. Saed's manuscript.⁷⁹ Reviewer #1 writes, "The first bulleted highlight [the Journal requires a list of bulleted highlights of research papers submitted for publication], 'Oxidative stress is a key mechanism to the initiation and progression of ovarian cancer' is not supported by this investigation and should be omitted."⁸⁰ Reviewer #2 writes, "While changes in redox potential play an important role in in tumor biology in general, the present data are insufficient to back up the claim that talcum is central to the development of ovarian cancer."⁸¹

Finally, Dr. Saed appears to take for granted that ovarian cancer is caused by inflammation, but this, too, has not been established. Dr. Saed essentially ignores the body of science suggesting that chronic inflammation does not play a role in the development of ovarian cancer,⁸² as well as

⁷⁴ Keskin N et al., *Does long-term talc exposure have a carcinogenic effect on the female genital system of rats? An experimental pilot study*. Arch Gynecol Obstet. (2009) 280(6):925-31.

⁷⁵ Saed Dep. Vol. I 50:10-13.

⁷⁶ Manuscript at 8.

⁷⁷ *Id.* (citing Kunz G et al., *The uterine peristaltic pump. Normal and impeded sperm transport within the female genital tract*. Adv Exp Med Biol. (1997) 424:267-77; Leyendecker G et al., *Uterine peristaltic activity and the development of endometriosis*. Ann NY Acad Sci. (2004) 1034:338-55; Zervomanolakis I et al., *Physiology of upward transport in the human female genital tract*. Ann NY Acad Sci. (2007) 1101:1-20

⁷⁸ Heller et al., *The relationship between perineal cosmetic talc usage and ovarian talc particle burden*. Am J Obstet Gynecol. (1996) 174(5):1507-10.

⁷⁹ Gynecologic Oncology Decision at 2-3.

⁸⁰ *Id.* at 2.

⁸¹ *Id.*

⁸² Malmberg K et al., *Serous tubal intraepithelial carcinoma, chronic fallopian tube injury, and serous carcinoma development*. Virchows Arch. (2016) 468(6):707-13; Rasmussen et al., *Pelvic inflammatory disease and the risk*
(cont'd)

studies that considered whether aspirin use and anti-inflammatory drugs reduced the risk of ovarian cancer,⁸³ with mixed results. As the Malmberg study concluded after finding no significant correlation between histological signs of inflammation and serous ovarian cancer, “Additional studies are needed to further evaluate the role of inflammation in carcinogenesis in the fallopian tube and its clinical implications of preventing serous carcinoma.”⁸⁴

Need for Further Study: In addition to the concerns noted above regarding the limitations of the studies performed *in vitro*, and the inappropriate conclusions drawn from them, several related types of studies were notably *not* performed by Dr. Saed in the context of providing evidence central to the fundamental assertion of plaintiffs that perineal talc use causes ovarian cancer. It is widely accepted in the cancer research community that there are several relatively straightforward assays that may be used to support the hypothesis that “normal” cells cultured *in vitro* have been stimulated by some type of exposure or manipulation (talc treatment in this case) to progress toward, or to fully develop, a neoplastic phenotype. These assays include, but are not limited to, the assessment of loss of contact inhibition by cells cultured in a petri dish *in vitro*, the acquisition of anchorage independent growth potential (as assessed by culturing cells in suspension in soft agar), and perhaps the most compelling experiment, demonstrating that the treated cells have obtained neoplastic potential as assessed by their ability to form tumors following subcutaneous injection into athymic (“nude”) mice. All these assays employ standard, well-established methodologies, and could have been readily performed by Dr. Saed using the “normal” cell lines described in his studies. As discussed earlier, none of these studies could have been performed using the three ovarian carcinoma cell lines described, however, since they have already undergone neoplastic transformation (in the humans from whence these cancers arose, and from whence the cell lines were derived). Notably, the three ovarian carcinoma cell lines could have been used as positive controls for the three assays described above, as they would have certainly demonstrated loss of contact inhibition in a petri dish, anchorage independent growth in soft agar, and tumorigenicity in athymic mice. I note that Dr. Saed himself proposed to do the second assay just mentioned involving suspension in soft agar, even stating in his proposal that actually demonstrating “neoplastic transformation” would be “critical in establishing a cause and effect relationship” between talc exposure and ovarian cancer,⁸⁵ but as he confirmed at his deposition, he never performed such a study.⁸⁶

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of ovarian cancer and borderline ovarian tumors: A pooled analysis of 13 case-control studies. *Am J Epidemiol.* (2017) 185(1): 8–20; Zhou et al., *Pelvic inflammatory disease and the risk of ovarian cancer: a meta-analysis.* *Cancer Causes Control.* (2017) 28(5):415-28.

⁸³ Ni X et al., *Meta-analysis on the association between non-steroidal anti-inflammatory drug use and ovarian cancer.* *Br J Clin Pharmacol.* (Jan. 2013) 75(1):26-35.

⁸⁴ Malmberg et al. (2016) at 712.

⁸⁵ Saed Dep. Vol. II, Ex. 44 at 3, *The Role of Talc Powder Exposure in Ovarian Cancer: A Mechanistic Approach.*

⁸⁶ Saed Dep. Vol. II 513:6-14.

D. Concerns Regarding Data and Handling/Manipulation of Laboratory Notebooks Generally

I have carefully studied three PDF files (in color) representing scanned portions of laboratory notebooks pertaining to the studies discussed in this Expert Report, that were provided by Dr. Saed, as well as Dr. Saed's deposition testimony about the conduct of his studies. My understanding is that the three PDF files accurately reflect the contents of some portion of the laboratory notebooks related to the studies discussed herein, and that the content of the notebooks was produced by Dr. Saed or members of the Saed laboratory working under his supervision. As a result of miscalculations, changing of dates on particular pages, whiting-out of data or notes, addition of data or notes to certain pages on different dates, the taping of data sheets cut from another source over data or notes previously existing on certain pages, the presence of data and other information in these notebooks that contradict Dr. Saed's statements during deposition as well as data and conclusions reached in the manuscript describing these studies that were submitted to at least two biomedical journals, and other irregularities too numerous to describe in detail, I have reached the following conclusions: 1) Some of the data and handwritten notes in these notebooks were intentionally manipulated; 2) Some of the data in these notebooks were selectively excluded from the final conclusions ultimately manifest in the manuscript submitted for publication; 3) Some of the data in these notebooks and conclusions drawn from them are internally inconsistent; 4) The handling of these laboratory notebooks and the recording of data and notes therein are egregiously inconsistent with the very minimum of well-accepted standard operating procedures with respect to the handling of laboratory notebooks and the recording of data and notes in the context of laboratory research; and, 5) *It is my expert (as defined on pages 2 and 3 of this Report) opinion that some of the data in these notebooks are at the very least unreliable, and at worst fabricated, and that the conclusions drawn from these data, as a whole, are thus unbelievable and essentially worthless with respect to the written and stated claims relating to a possible mechanism(s) through which talc may induce tumorigenesis in cultured cells specifically, and by multiple layers of illogical extension, through which talc may induce ovarian cancer in women exposed to talc generally.*

For the record, I received three notebook files. The first ("Expert Report Notebook Files") was described as the laboratory notebook that relates to Dr. Saed's work for his expert report. It consists of 97 pages (with what would appear to be printed stickers in the bottom corner of each page labeled SAED000001(color) – SAED000097(color)). There are handwritten numbers on the bottom corner of each page, beginning with "30" on page 1 and "124" on page 97. There are two un-numbered pages inserted between the handwritten pages 33 and 35, and one un-numbered page inserted between the handwritten pages 39 and 40, possibly accounting for the discrepancy of two "missing" pages with respect to the handwritten numbered version. For orientation, page 1 (or 30) contains color photographs of the front and back of a commercial container of "Johnson's baby powder."

The second laboratory notebook file ("Abstract Lab Notebook Files") contains a table of contents on the un-numbered first page, with a series of dates, 9/26/2017 – 10/20/2017, descending vertically on the left side, and page numbers from 38-63 descending vertically on the right side. The pages are hand-numbered in the bottom corner, beginning with 38 after the TOC

page and ending with 61, prior to the last page consisting of a scientific poster prepared for presentation.

The third laboratory notebook file (“Preliminary Work Notebook Files”) represents the first 30 pages that are missing from the Expert Report Notebook Files. My understanding is that plaintiffs did not originally share it with defendants because they characterized it as containing only preliminary work.⁸⁷ It begins with a table of contents on the un-numbered first page, with a series of dates, 10/15/2017 – 10/6/2017, descending vertically on the left side, and page numbers from 1-124 descending vertically on the right side. Pages 25-30 are missing from the table of contents. The pages are hand-numbered in the bottom corner, beginning with 1 after the TOC page containing a photograph of a container of “Talc” from Fisher Chemical. The next page is un-numbered and contains the same color photographs of a commercial container of “Johnson’s baby powder” that appeared in the Expert Report Notebook Files. The next page is numbered 2 and the rest are numbered consecutively 3-24.

Examples of some of the irregularities described in the first paragraph of section IV.D of this Expert Report (above) include:

1) Pages from another source taped onto the laboratory notebook page, white-out present in both files, including dates whited out and single entries that are made with ink of a different color than the text otherwise filling the same page. I further note that apparent manipulation of the dates has resulted not only in lab books that have entries out of chronological order, but also statements that cannot possibly be true. For example, page 25 of the Expert Report Notebook Files is dated January 7, 2018, and claims to be recording protein extractions from samples 356 to 386.⁸⁸ The first line after the top of this page states that the cells were seeded on January 3, 2018.⁸⁹ The very next page identifies samples 356 through 386.⁹⁰ But exactly the same samples are also identified on page 20 of the Preliminary Work Notebook Files (which, as I note above, plaintiffs initially withheld from production on the ground that it was unrelated work). *That* page refers to the actual seeding of the samples and is dated *February 1, 2018* – or *nearly a month after* protein extractions were supposedly taken from the same samples (which had not been created yet).⁹¹ There is no question that these pages in the separate parts of the Notebooks are referring to the same samples – Dr. Saed said so himself at his deposition, calling the samples “exactly the same.”⁹² In fact, the February 1 date in the Preliminary Work Notebook Files follows a “1/3” date that has been crossed out⁹³ – a date that matched the date referred to on page

⁸⁷ Saed Dep. Vol. I 13:18-14:10, 15:24-16:1.

⁸⁸ Saed Dep. Vol. I, Ex. 1 at SAED000025(color).

⁸⁹ *Id.*

⁹⁰ *Id.* at SAED000026(color).

⁹¹ Saed Dep. Vol. II, Ex. 23 at Ghassan Saed’s Talc Study Lab Notebook – Preliminary Study (“Preliminary Work Notebook Files”) at 20.

⁹² Saed Dep. Vol. II 390:7-17.

⁹³ Preliminary Work Notebook Files at 20.

25 of the Expert Report Notebook Files⁹⁴ as the date when the cells were supposedly seeded. These changes suggest that the dates were intentionally manipulated (rather than, for example, that the author mistakenly believed that it was January 3 on February 1).

2) Throughout the Preliminary Work Notebook Files, the handwritten page numbers are invariably smudged, suggesting either erasure and writing over, or white-out and writing over.

3) On page 19 of the Preliminary Work Notebook Files, there is a handwritten entry as follows: “1/31/18 – The presence of 1000 µg/ml is physically killing the cells. – We need to decrease dose.”⁹⁵ In none of the pages preceding page 19 of the Preliminary Work Notebook Files, or in any section of the Abstract Lab Notebook Files (containing experiments ostensibly performed prior to 1/31/18), is there evidence of such toxicity. In fact, data related to gene expression (as assessed by RNA levels) are readily obtained at doses of 20, 100 and 1000 µg/ml. In some cases, gene expression of particular enzymes is higher at 1000 µg/ml than at 20 or 100 µg/ml, inconsistent with cells being “physically killed” at 1000 µg/ml. In addition, the amount of RNA obtained from a given number of cells is similar in control vs. treated cells, and from cells treated at various doses (20 – 1000 µg/ml). These data are also inconsistent with a greater proportion of “dead” cells at 1000 µg/ml. What is *clearly* apparent, however, is that gene expression and CA-125 secretion levels at a dose of 1000 µg/ml do not follow a traditional “dose-response” (a biological response becoming increasingly higher or lower in response to an increasing dose of test substance). In quantitating CA-125 secretion, for example, sometimes the amount does not change with talc, sometimes it is lower with talc, and sometimes it is higher with talc, compared to DMSO control treatment of the same cells.⁹⁶ This phenomenon does not fit with a central tenet of Dr. Saed’s conclusion, which is that there is a clear dose-dependent response in terms of gene expression, protein “activity,” CA-125 secretion, etc., following talc exposure. This selective exclusion of data in order to fit data to a particular hypothesis or conclusion, “cherry-picking” data to use a colloquialism, is unsound scientific methodology of the highest order.

4) With respect to data points themselves, there is clear evidence of error (human or machine) in terms of simple arithmetic calculations. For example, in a random spot check (by me) of raw data in the Expert Report Lab Notebook Files, consider the computer-generated table (whether populated by a human or a machine being impossible to know) on page SAED000033(color). These data relate to an ELISA-based measurement of catalase “protein/activity” following exposure of cultured cells to talc at doses of only 5, 20 and 100 µg, (presumably per ml?) and the table is dated 1/11/18.⁹⁷ This date is 20 days before 1/31/18, the date upon which, in the

⁹⁴ Saed Dep. Vol. I, Ex. 1 at SAED000025(color).

⁹⁵ Preliminary Work Notebook Files at 19.

⁹⁶ For example, see Preliminary Work Notebook Files at 13.

⁹⁷ Saed Dep. Vol. I, Ex. 1 at SAED000033(color).

Preliminary Work Notebook Files, a notation is found that, “The presence of 1000 µg/ml is physically killing the cells...”⁹⁸

Regardless, if one considers the data table in question, the first horizontal row concludes on the far right with an “Average” value of 11.07 for three replicate values of 9.98, 11.63, and 10.50.⁹⁹ The correct average would have been 10.70. In horizontal line two of the same table, the “Average” value is listed as 9.13 for three replicate values of 9.18, 10.64, and 9.09.¹⁰⁰ The correct average would have been 9.64. Thus, the recorded difference between “control” A2780 cells and talc-treated (5 µg) A2780 cells is 1.94 nmol/min/ml¹⁰¹; the actual difference is 1.06 nmol/min/ml, a much smaller difference. A “larger difference” in this case would have been more consistent with the experimental hypothesis and conclusions, which of course could be simply coincidental, the arithmetic errors notwithstanding. There are other examples of these kinds of data errors throughout Dr. Saed’s work, several of which were covered at his second deposition.¹⁰²

5) I have also reviewed multiple drafts of Dr. Saed’s manuscript, including the version of it that was rejected by *Gynecologic Oncology* and the version later accepted by *Reproductive Sciences*. Of particular interest is the fact that the earlier submission to *Gynecologic Oncology* claimed to have observed effects of talc after only 48 hours of treatment – a fact directly addressed by one of the reviewers in the rejection letter, who wrote that the “fact that SNPs were changed following such short exposure to talcum is surprising and makes one wonder what the biological effect of such changes might be.”¹⁰³ Curiously, Dr. Saed’s subsequent submission to *Reproductive Sciences* changed the stated time of treatment to 72 hours – but includes many of the same tables that were included in the submission to *Gynecologic Oncology*, with exactly the same data for each dose of treatment, but with the exposure period changed from 48 hours to 72 hours. And Dr. Saed’s report states that he treated talc “for 48 hours”¹⁰⁴ – a discrepancy from his latest manuscript that he attempted to explain as “a typo” in his report at his deposition.¹⁰⁵ Of course, another possibility is that Dr. Saed decided that 72 hours of treatment would appear more credible and that he simply revised this reference in his manuscript without rerunning the experiments before he resubmitted but forgot to make the same change to his report.

⁹⁸ Preliminary Work Notebook Files at 19.

⁹⁹ Saed Dep. Vol. I, Ex. 1 at SAED000033(color).

¹⁰⁰ *Id.*

¹⁰¹ *Id.* at SAED000090(color).

¹⁰² *See, e.g.*, Saed Dep. Vol. II 450:24-452:6, 452:22-453:24 (additional averaging errors).

¹⁰³ Gynecologic Oncology Decision at 2.

¹⁰⁴ Saed Rep. at 14.

¹⁰⁵ Saed Dep. Vol. I 185:6-186:7.

E. Additional Concern

Improper financial disclosure: Dr. Saed’s insufficient conflict-of-interest disclosure violates publishing principles and further indicates that his opinions are not reliable. Although there is no single definitive standard for an appropriate conflict-of-interest disclosure, failures to disclose conflicts of interest have undermined the faith of both the public and healthcare professionals in the quality of scientific and medical literature.¹⁰⁶ As such, most reputable journals have developed their own conflict-of-interest disclosure policies, and various voluntary organizations have advanced model standards that function as persuasive guidelines. Dr. Saed’s minimal disclosure violates both these model policies and the policy in place at *Reproductive Sciences*,¹⁰⁷ the journal in which his manuscript is to be published.

For example, the International Committee of Medical Journal Editors states that authors should disclose “all financial or personal relationships that might bias or be seen to bias their work” and, in particular, notes “[f]inancial relationships (such as . . . paid expert testimony)” as the most obvious type of conflict of interest.¹⁰⁸ The World Association of Medical Editors has set forth a similar policy.¹⁰⁹ In keeping with these principles, *Reproductive Sciences* requires all authors to make a “specific” declaration of “any financial relationship” that the author has and the “interests” of the sponsoring organization, and to include any information “that might represent an appearance of a conflict of interest” in the cover letter.¹¹⁰ Dr. Saed admits that he did not include any such information in his cover letter.¹¹¹ Dr. Saed did acknowledge elsewhere that he “acted as a consultant regarding this topic for a fee.”¹¹² He did not link his consultancy to his manuscript in any way, much less disclose that plaintiffs’ counsel funded the specific study that he submitted. Nor did he disclose that he functioned as more than a consultant, but as a testifying expert witness. Indeed, he did not even disclose for whom he consulted – whether it was a party, such as plaintiffs’ counsel, with an interest in showing talc to be dangerous, a party, such as an industry player, with an interest in showing talc to be safe, or an unbiased organization. Therefore, reviewers, and ultimately readers, could not evaluate his conclusions with appropriate context in mind.

¹⁰⁶ Blum JA et al., *Requirements and definitions in conflict of interest policies of medical journals*. JAMA. (2009) 302(20):2230-4.

¹⁰⁷ See Saed Dep. Vol. I, Ex. 12 at 3 (Sage Publishing Reproductive Sciences Webpage); see also Sage Publications, Declaration of Conflicting Interests Policy (2019), <https://us.sagepub.com/en-us/nam/declaration-of-conflicting-interests-policy>.

¹⁰⁸ Int’l Committee Med. J. Editors, *Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals* 3, <http://www.icmje.org/icmje-recommendations.pdf> (updated Dec. 2018).

¹⁰⁹ See World Ass’n of Med. Editors, *Conflict of Interest in Peer-Reviewed Medical Journals*, <http://wame.org/conflict-of-interest-in-peer-reviewed-medical-journals> (updated July 25, 2009).

¹¹⁰ See Saed Dep. Vol. I, Ex. 12 at 3; see also Sage Publications, Declaration of Conflicting Interests Policy.

¹¹¹ Saed Dep. Vol. I 156:10-19.

¹¹² *Id.* 144:2-7; see also *id.* 142:1-2.

V. MATERIALS CONSIDERED

1. A2780 Cell Line human,
https://www.sigmaaldrich.com/catalog/product/sigma/cb_93112519?lang=en®ion=US
2. Belotte J et al., *A single nucleotide polymorphism in catalase is strongly associated with ovarian cancer survival*. PLoS One. (2015) 24;10(8):e0135739
3. Blum JA et al., *Requirements and definitions in conflict of interest policies of medical journals*. JAMA. (2009) 302(20):2230-4
4. Chu H et al., *The MPO -463G>A polymorphism and cancer risk: a meta-analysis based on 43 case-control studies*. Mutagenesis. (2010) 25(4):389-95
5. Deposition of Ghassan Saed, Ph.D., Vol. I, Jan. 23, 2019 (MDL No. 2738)
6. Deposition of Ghassan Saed, Ph.D., Vol. II, Feb. 14, 2019 (MDL No. 2738)
7. Didžiapetrienė J et al., *Significance of blood serum catalase activity and malondialdehyde level for survival prognosis of ovarian cancer patients*. Medicina (Kaunas) (2014) 50(4):204-8
8. Endo-Capron S et al., *In vitro response of rat pleural mesothelial cells to talc samples in genotoxicity assays (sister chromatid exchanges and DNA repair)*. Toxicol In Vitro. (1993) 7(1):7-14
9. Expert Report of Daniel L. Clarke-Pearson, M.D. Nov. 16, 2018 (MDL No. 2738)
10. Expert Report of Ghassan Saed, M.D., Nov. 16, 2018 (MDL No. 2738)
11. Expert Report of Judith Wolf, M.D. Nov. 16, 2018 (MDL No. 2738)
12. Expert Report of Sarah Kane, M.D., Nov. 15, 2018 (MDL No. 2738)
13. Expert Report of Shawn Levy, Ph.D., Nov. 16, 2018 (MDL No. 2738)
14. Fletcher NM et al., LB-044 – Talcum Powder Enhances Cancer Antigen 125 Levels in Ovarian Cancer Cells and in Normal Ovarian Epithelial Cells (abstract) (2018) (Ex. 21 to Deposition of Ghassan Saed, Ph.D., Jan. 23, 2019 (MDL No. 2738))
15. Fletcher NM et al., Molecular basis supporting the association of talcum powder use with increased risk of ovarian cancer (2019) (unpublished manuscript) (Ex. 8 to Deposition of Ghassan Saed, Ph.D., Jan. 23, 2019 (MDL No. 2738))
16. Fletcher NM et al., *Specific point mutations in key redox enzymes are associated with chemoresistance in epithelial ovarian cancer*. Free Radic Biol Med. (2016) 102:122-32
17. Fletcher NM et al., Talcum Powder Enhances Oxidative Stress in Ovarian Cancer, Reproductive Sciences, Vol. 25, Suppl. 1, F-098 (abstract) (2018) (Ex. 20 to Deposition of Ghassan Saed, Ph.D., Jan. 23, 2019 (MDL No. 2738))
18. Forsberg L et al., *A common functional C-T substitution polymorphism in the promoter region of the human catalase gene influences transcription factor binding, reporter gene*

- transcription and is correlated to blood catalase levels.* Free Radic Biol Med. (2001) 30(5):500-5
19. Ghassan Saed's PCR EOC SRI Notebook (Ex. 9 to Deposition of Ghassan Saed, Ph.D., Jan. 23, 2019 (MDL No. 2738))
 20. Ghassan Saed's Talc Study Lab Notebook – Preliminary Study (Ex. 23 to Deposition of Ghassan Saed, Ph.D., Feb. 14, 2019 (MDL No. 2738))
 21. Gynecologic Oncology Email dated Sept. 19, 2018 re: GYN-18-1020: Final Decision (Ex. 35 to Deposition of Ghassan Saed, Ph.D., Feb. 14, 2019 (MDL No. 2738))
 22. Hall MD et al., *Say No to DMSO: Dimethyl sulfoxide inactivates cisplatin, carboplatin and other platinum complexes.* Cancer Res. (2014) 74(14):3913-22
 23. Hamilton TC et al., *Effects of talc on the rat ovary.* Br J Exp Pathol. (1984) 65(1):101-6
 24. Harper & Saed, Talc Induces a Pro-Oxidant State in Normal and Ovarian Cancer Cells Through Gene Point Mutations in Key Redox Enzymes (Ex. 19 to Deposition of Ghassan Saed, Ph.D., Jan. 23, 2019 (MDL No. 2738))
 25. Heller DS et al., *The relationship between perineal cosmetic talc usage and ovarian talc particle burden.* Am J Obstet Gynecol. (1996) 174(5):1507-10
 26. Henderson WJ et al., *Talc and carcinoma of the ovary and cervix.* J Obstet Gynaecol Br Commonw. (1971) 78(3):266-72
 27. Int'l Agency for Research on Cancer, *Monographs on the Evaluation of Carcinogenic Risks to Humans* Vol. 93: Carbon Black, Titanium Dioxide, and Talc (2010)
 28. Int'l Committee Med. J. Editors, *Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals*, <http://www.icmje.org/icmje-recommendations.pdf> (updated Dec. 2018)
 29. Jacobs I et al., *Ovarian cancer screening and mortality in the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS): a randomized controlled trial.* Lancet (2016) 387:945-56
 30. Keskin N et al., *Does long-term talc exposure have a carcinogenic effect on the female genital system of rats? An experimental pilot study.* Arch Gynecol Obstet. (2009) 280(6):925-31
 31. Klaunig JE et al., *Oxidative stress and oxidative damage in chemical carcinogenesis.* Toxicol Appl Pharmacol (2011) 25:86-99
 32. Kuchenbaecker KB et al., *Identification of six new susceptibility loci for invasive epithelial ovarian cancer.* Nat Genet. (2015) 47(2):164-71
 33. Kuchenbaecker KB et al., *Risks of breast, ovarian, and contralateral breast cancer for BRCA1 and BRCA2 mutation carriers.* JAMA (2017) 317(23):2402-16
 34. Lab Notebook, SAED000001(color)-SAED000097(color) (Ex. 1 to Deposition of Ghassan Saed, Ph.D., Jan. 23, 2019 (MDL No. 2738))

35. Malmberg K et al., *Serous tubal intraepithelial carcinoma, chronic fallopian tube injury, and serous carcinoma development*. Virchows Arch. (2016) 468(6):707-13
36. Ni X et al., *Meta-analysis on the association between non-steroidal anti-inflammatory drug use and ovarian cancer*. Br J Clin Pharmacol. (2013) 75(1):26-35
37. Norquist BM et al., *Inherited mutations in women with ovarian carcinoma*. JAMA Oncol. (2016) 2(4):482-90
38. Pharoah PD et al., *GWAS meta-analysis and replication identifies three new susceptibility loci for ovarian cancer*. Nat Genet. (2013) 45(4):362-70
39. Quick SK et al., *Effect modification by catalase genotype suggests a role for oxidative stress in the association of hormone replacement therapy with postmenopausal breast cancer risk*. Cancer Epidemiol Biomarkers Prev. (2008) 17(5):1082-7
40. Rasmussen et al., *Pelvic inflammatory disease and the risk of ovarian cancer and borderline ovarian tumors: A pooled analysis of 13 case-control studies*. Am J Epidemiol. (2017) 185(1):8–20
41. Sage Publications, Declaration of Conflicting Interests Policy (2019), <https://us.sagepub.com/en-us/nam/declaration-of-conflicting-interests-policy>
42. Sage Publications, Reproductive Sciences (Ex. 12 to Deposition of Ghassan Saed, Ph.D., Jan. 23, 2019 (MDL No. 2738))
43. Scholler N & Urban N, *CA125 in ovarian cancer*. Biomark Med (2007) 1(4):513-23
44. SK-OV-3 [SKOV-3; SKOV3] (ATCC® HTB-77™), <https://www.atcc.org/products/all/HTB-77.aspx>
45. The Role of Talc Powder Exposure in Ovarian Cancer: A Mechanistic Approach (Ex. 43 to Deposition of Ghassan Saed, Ph.D., Feb. 14, 2019 (MDL No. 2738))
46. Tomasetti C & Vogelstein B, *Variation in cancer risk among tissues can be explained by the number of stem cell divisions*. Science (2015) 347:78-81, 2015
47. TOV-112D (ATCC® CRL-11731™), <https://www.atcc.org/products/all/CRL-11731.aspx>
48. Walsh T et al., *Mutations in 12 genes for inherited ovarian, fallopian tube, and peritoneal carcinoma identified by massively parallel sequencing*. Proc Natl Acad Sci USA (2011) 108(44):18032-7
49. World Ass'n of Med. Editors, *Conflict of Interest in Peer-Reviewed Medical Journals*, <http://wame.org/conflict-of-interest-in-peer-reviewed-medical-journals> (updated July 25, 2009)
50. Zhou et al., *Pelvic inflammatory disease and the risk of ovarian cancer: a meta-analysis*. Cancer Causes Control. (2017) 28(5):415-28

EXHIBIT A

Curriculum Vitae (02/04/19)

Name: Jeff Boyd

Place of Birth: Chapel Hill, NC

Nationality: USA

Office Address: Herbert Wertheim College of Medicine
Florida International University
11200 SW 8th Street, AHC2-693
Miami, FL 33199
Tel: 305-348-0646
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Miami Cancer Institute
Baptist Health South Florida
8900 North Kendall Drive
Miami, FL 33176
Tel: 786-527-8023
E-mail: JeffBo@BaptistHealth.net

Home Address: 505 Luenga Avenue
Coral Gables, FL 33146

Education: Duke University, Durham, NC
B.S. (Psychology/Chemistry), 1980

NC State University, Raleigh, NC
M.S. (Toxicology/Biochemistry), 1982

NC State University, Raleigh, NC
Ph.D. (Toxicology/Biochemistry), 1986

Postdoctoral Training: 1986-1988: Environmental Pathology Fellowship
Department of Pathology
Lineberger Comprehensive Cancer Center
University of North Carolina School of Medicine
Chapel Hill, NC

1988-1990: Senior Staff Fellow
Cellular Carcinogenesis Section
Laboratory of Molecular Carcinogenesis
NIH/National Institute of Environmental Health Sciences
Research Triangle Park, NC

Positions and Appointments:

1990-1994: Head, Gynecologic Pathobiology Section
Laboratory of Molecular Carcinogenesis
NIH/National Institute of Environmental Health Sciences
Research Triangle Park, NC

1992-1994: Adjunct Assistant Professor (concurrent with primary position above)
Department of Epidemiology
University of North Carolina School of Public Health
Chapel Hill, NC

1994-1997: Associate Professor
Department of Obstetrics and Gynecology and Department of Genetics
Director, Gynecologic Oncology Research Laboratory
Member, Comprehensive Cancer Center
Member, Center for Research on Women's Health and Reproduction
Associate Member, Institute for Human Gene Therapy
University of Pennsylvania
Philadelphia, PA

1997-2003: Associate Attending Biologist
Gynecology Service, Department of Surgery
Clinical Genetics Service, Department of Medicine
Director, Gynecology and Breast Research Laboratory
Memorial Hospital for Cancer and Allied Diseases
Associate Member, Memorial Sloan-Kettering Cancer Center
New York, NY

2003-2006: Attending Biologist
Gynecology Service, Department of Surgery
Clinical Genetics Service, Department of Medicine
Director, Gynecology and Breast Research Laboratory (Department of Surgery)
Director, Diagnostic Molecular Genetics Laboratory (Department of Medicine)
Memorial Hospital for Cancer and Allied Diseases
Member (with tenure-of-title), Memorial Sloan-Kettering Cancer Center
New York, NY

2006-2007: Vice President, Laboratory Science
2007-2008: Vice President, Oncology and Research
2007-2008: Director, Curtis and Elizabeth Anderson Cancer Institute
2006-2008: Professor of Obstetrics and Gynecology, Surgery, Medicine, and Division of
Basic Medical Sciences, Mercer University School of Medicine - Savannah
Assistant Dean for Research, Mercer University School of Medicine - Savannah
Distinguished Cancer Scholar, State of Georgia
Memorial University Medical Center, Savannah, GA

2008-2010: Senior Vice President and Chief Scientific Officer
Robert C. Young, MD, Chair in Cancer Research
Professor (with tenure), Women's Cancer Program
Fox Chase Cancer Center, Philadelphia, PA

2010-2014: Senior Vice President, Molecular Medicine
Robert C. Young, MD, Chair in Cancer Research
Executive Director, Cancer Genome Institute
Chief, Division of Molecular Pathology
Professor (with tenure), Cancer Biology Program
Fox Chase Cancer Center, Philadelphia, PA

2008-2015: Professor (with tenure), Cancer Biology Program
Robert C. Young, MD, Chair in Cancer Research
Fox Chase Cancer Center, Philadelphia, PA

2015-present: Professor (with tenure) and Chair, Department of Human and Molecular
Genetics
Professor, Department of Obstetrics and Gynecology
Associate Dean for Basic Research and Graduate Programs
Herbert Wertheim College of Medicine
Florida International University
Miami, FL

2015-present: Associate Deputy Director, Translational Research and Genomic Medicine
Miami Cancer Institute
Baptist Health South Florida
Miami, FL

Scientific and Medical Societies:

American Association for the Advancement of Science (1982)
American Association for Cancer Research (1990)
American Society for Cell Biology (1992)
American Society of Clinical Oncology (2002)
American Society of Human Genetics (1997)
Association for Molecular Pathology (2014)
International Society of Gynecologic Oncology (2006)
Society of Gynecologic Oncology (1997)

Awards, Fellowships, and Grants:

Award for Special Achievement
Department of Health, Education, and Welfare, NIH, July, 1980.

Environmental Pathology Training Fellowship (Institutional NRSA)
NIH/NIEHS, T32-ES07017, March, 1986.

National Research Service Award (Individual)
NIH/NCI, F32-CA0524, February, 1988.

Co-Principal Investigator, Gynecologic Cancer Foundation/Karin Smith Award,
“Gene Therapy of Ovarian Cancer” (Univ of Pennsylvania); 6/1/96-5/31/97;
\$50,000 total direct costs.

Principal Investigator, “Molecular Genetics of Gynecologic Cancers”
NIH/NCI, R01-CA67164; 10/1/96-9/30/00; \$482,401 total direct costs.

Principal Investigator, “Genetic Mechanism of BRCA1-Linked Ovarian Tumorigenesis”,
NIH/NCI, R01-CA71840, 10/1/96-9/30/00; \$465,563 total direct costs.

Principal Investigator, “Genetic Mechanism of BRCA-Linked Ovarian Tumorigenesis”,
NIH/NCI, R01-CA71840, 2/1/01-1/31/05; \$676,000 total direct costs.

Principal Investigator, “Basic and Translational Research Program in the Molecular
Genetics of Gynecologic and Breast Cancers: New Strategies for Prevention, Early
Detection, and Treatment”, Keck Foundation; 1/1/99-12/31/03; \$2,500,000 direct costs.

Principal Investigator, “Molecular Classification of Ovarian Cancers”,
NIH/NCI, U01-CA88175; 10/1/00-9/30/05; \$655,976 total direct costs.

Principal Investigator, “Preclinical Alterations in Breast Epithelium of BRCA Heterozygotes”, Breast Cancer Research Foundation, 10/1/00; \$170,000 total direct costs.

Principal Investigator, “Molecular Genetic Basis of Invasive Breast Cancer Risk Associated with Lobular Carcinoma in Situ”, Breast Cancer Research Foundation, 10/1/01; \$243,356 total direct costs.

Principal Investigator, “Prediction of Breast Cancer Risk by Gene Expression Profiling”, Breast Cancer Alliance, 11/1/01; \$130,000 total direct costs.

Principal Investigator, “Molecular Response to Selective Estrogen Receptor Modulators (SERMs) in Human Breast Cancer Cells”, Breast Cancer Research Foundation, 10/1/02; \$228,862 total direct costs.

Principal Investigator, “Genetic Polymorphisms and Risk of Breast Cancer”, Breast Cancer Alliance, 11/1/02; \$91,592 total direct costs.

Principal Investigator, “Somatic Genetic Alterations in *BRCA*-Linked Human Breast Cancer”, Breast Cancer Research Foundation, 10/1/03; \$230,000 total direct costs.

Principal Investigator, “Molecular Classification of Endometrial Cancers”, NIH/NCI, R01-CA100272; 4/1/04-3/31/08; \$1,350,000 total direct costs.

Principal Investigator, “Prediction of Breast Cancer Risk by Whole Genome Profiling”, Department of Defense, CDMRP, BC033728; 8/1/04-7/31/05; \$75,000 total direct costs.

Principal Investigator, “Prediction of Breast Cancer Risk by Whole Genome Profiling”, Breast Cancer Research Foundation, 10/1/04; \$250,000 total direct costs.

Project Director, “Project 1: Role of CA125/MUC16 in Ovarian Tumorigenesis”, NIH/NCI, P01-CA52477-13, “Epithelial Ovarian Cancer Program Project”; 4/1/05-3/31/10; \$7,374,628 total direct costs.

Co-Principal Investigator, “Polygenic Basis of Breast Cancer”, Breast Cancer Research Foundation, 10/1/05; \$250,000 total direct costs.

Georgia Distinguished Cancer Scholar, Georgia Cancer Coalition, 2006-2010; \$750,000 total direct costs.

Principal Investigator, “Recruiting shRNA Functional Screening Expertise”, Pennsylvania Department of Community and Economic Development Grant, C000043689, 1/1/09-6/30/10; \$150,000 total costs.

Principal Investigator, American Cancer Society Institutional Research Grant, IRG-92-027-15, 1/1/08-12/31/10; \$360,000 total costs.

Principal Investigator, “The Exomes of Ovarian Tumors of Low Malignant Potential and Low Grade Ovarian Cancers”, Sandy Rollman Ovarian Cancer Foundation; 6/1/10-5/31/11; \$60,000 direct costs.

Mentor, “Determine the Role of Canonical Wnt Signaling in Ovarian Tumorigenesis”, CDMRP/DOD, Ovarian Academy Award W81XWH-10-1-0823 (PI: R Zhang), 9/15/10-3/29/13; \$750,000 total direct costs.

Angela Carlino Excellence in Ovarian Cancer Research Award, Sandy Rollman Ovarian Cancer Foundation; October, 2010.

Principal Investigator, “The Transcriptome of Platinum Resistance in Ovarian Cancer”, The Carpenter Foundation; 7/1/12-6/30/13; \$50,000 total direct costs.

Principal Investigator, “FCCC-PENN SPORE in Ovarian Cancer”, NIH/NCI, P50 CA083638; 8/21/09–5/31/15; \$9,996,150 total direct costs.

Mentor, “Identifying Determinants of PARP Inhibitor Sensitivity in Ovarian Cancer”, CDMRP/DOD, Ovarian Academy Award OC130212 (PI: N Johnson), 2/1/14-1/31/19; \$750,000 total direct costs.

Rosalind Franklin Award for Excellence in Ovarian Cancer Research, Ovarian Cancer Research Fund Alliance; July, 2016.

Co-Investigator, “The Impact of Radiation Dose on Brain Morphology, Volumetric Changes, Endocrine Function, and Neurocognitive Function Following Cranial Radiation Therapy in Children with Brain and Skull Base Tumors”, Florida Department of Health, Award 8LA04 (PI: M. Hall), 6/14/18-4/30/22; \$700,000 total direct costs.

Editorial Positions:

1993-1997:	Associate Editor, <i>Molecular and Cellular Differentiation</i>
1994-2006:	Associate Editor, <i>Molecular Carcinogenesis</i>
1997-2003:	Editorial Board, <i>Gynecologic Oncology</i>
2003-2008:	Associate Editor, <i>Gynecologic Oncology</i>
2004-2008:	Editorial Board, <i>Journal of Clinical Oncology</i>
2004-2017:	Editorial Board, <i>American Journal of Pathology</i>
2017-present	Editorial Board, <i>Anticancer Research</i>

Committee Assignments (Previous):

Member, Task Force for Activities and Membership Development,
American Association for Cancer Research, 1993.

Member, Epidemiology Committee, DOD Breast Cancer Program Review, 1994.

Member, Program Committee, Annual Meeting of the American Association for Cancer
Research, 1995.

Member, Physiology Committee, DOD Gulf War Illness Program Review, 1995.

Member, Reproductive Biology Committee, DOD Women's Health Program Review,
1996.

Member, Special Review Group, "Endocrine Disrupting Chemicals and Women's Health
Outcomes" (RFA 96-003), NIH/NIEHS, 1996.

Member, Epidemiology Committee, DOD Breast Cancer Program Review, 1996.

Invited Participant, American Cancer Society Workshop on Heritable Cancer Syndrome
and Genetic Testing, 1996.

Member, Special Review Panel for Program Project Application P01-CA73992,
"Molecular and Clinical Approaches to Colon Cancer Precursors", University of Utah,
1996.

Ad-Hoc Member, Program Committee, Society for Gynecologic Oncologists Annual
Meeting, 1997.

Invited participant, "The Strategic Planning Conference on New Directions in Ovarian
Cancer Research", The U.S. Public Health Service's Office on Women's Health,
Washington, DC, 1997.

Member, Committee for DOD Ovarian Cancer Program Review, 1998.

Invited participant, "Implementation Meeting for New Directions in Ovarian Cancer
Research", The National Cancer Institute and The Society of Gynecologic Oncologists,
Bethesda, MD, 1998.

Member, Special Review Panel for National Cancer Institute Program Project Grant
Application, "Epidemiologic and Genetic Studies of Breast Cancer", Mayo Foundation,
Rochester, MN, February, 1999.

Ad Hoc Member, National Cancer Institute Scientific Review Group, Subcommittee E (Prevention and Control), Bethesda, MD, 1999.

Ad-Hoc Member, Initial Review Group, Small Grants Program for Cancer Epidemiology, National Cancer Institute, Bethesda, MD, 1999.

Ad-Hoc Member, Peer Review Committee on Molecular Genetics and Oncogenes, American Cancer Society, 1999.

Member, Specified Appropriations Program Peer Review Committee, United States Army Medical Research and Material Command, 1999.

Member, Committee for DOD Ovarian Cancer Program Review, 1999.

Member, Special Review Panel for National Cancer Institute Program Project Grant Application, "DNA Repair Genes and Cancer", University of Kentucky Medical Center, Lexington, KY, September, 1999.

Member, Program Committee, Society of Gynecologic Oncologists Annual Meeting, 2000.

Member, Special Review Panel for National Cancer Institute Program Project Grant Application, "Dietary and Hormonal Determinants of Cancer in Women" (Nurses' Health Study), Brigham and Women's Hospital, Boston, MA, February, 2000.

Invited Participant, Gynecologic Cancer Translational Research Retreat (GOG/NCI), Chantilly, VA; May, 2000.

Course Director, Second International Conference on Ovarian Cancer, Memorial Sloan-Kettering Cancer Center, New York, NY; June, 2000.

Invited Participant, Conference on Ovarian Cancer Screening, NCI, Bethesda, MD; September, 2000.

Member, Committee for DOD Ovarian Cancer Program Review, 2000.

Invited Participant, NCI Gynecologic Cancers Progress Review Group Roundtable Meeting, Herndon, VA; June, 2001.

Member, Committee for DOD Ovarian Cancer Program Review, 2001.

Ad-Hoc Member, PTHC/CAMP Scientific Review Group, National Institutes of Health, Washington, DC; June, 2002.

Member, Epidemiology Panel, DOD Breast Cancer Program Review, 2002.

Member, Special Review Panel for National Cancer Institute Program Project Grant Application, “Cervical Cancer: Biology of Initiation and Progression”, Emory University, Atlanta, GA, September, 2002.

Member, Scientific Review Group for Ovarian SPORE Applications, National Cancer Institute, Bethesda, MD; June, 2003.

Invited participant, Borderline Ovarian Tumor Consensus Workshop, National Cancer Institute, Bethesda, MD; August, 2003.

Member, Special Emphasis Panel ZCA1 SRRB-4 J1 R, “Strategic Partnerships to Evaluate Cancer Signatures”, National Institutes of Health, 2004.

Member, Program Committee, Society of Gynecologic Oncologists Annual Meeting, Miami Beach, FL; 2005.

Ad-Hoc Member, NCI Scientific Review Group, Subcommittee E – Cancer Epidemiology, Prevention, and Control, Bethesda, MD; April, 2005.

Chair, Special Emphasis Panel, ZRG1 ONC-U (03), Breast and Ovarian Cancer Genetics, Center for Scientific Review, National Institutes of Health; July, 2005.

Invited Participant, National Cancer Institute Ovarian Cancer State-of-the-Science Meeting, Bethesda, MD; September, 2005.

Member, Education Committee, Society of Gynecologic Oncologists, 2000-2004
Member, Institutional Review Board, Memorial Sloan-Kettering Cancer Center, 1999-2006.

Member, Human Tissue Utilization Committee, Memorial Sloan-Kettering Cancer Center, 2002-2006.

Member, Computational Biology Program Search Committee, Memorial Sloan-Kettering Cancer Center, 2002-2006.

Member, Database Working Group, Memorial Sloan-Kettering Cancer Center, 2002-2006.

Ad-Hoc Member, Committee on Appointments and Promotions, Memorial Sloan-Kettering Cancer Center; July 2002, October, 2003, April, 2004, March, 2005.\

Member, Translational and Integrative Medicine Grant Review Committee, Memorial Sloan-Kettering Cancer Center; 2003-2006.

Member, Institutional Review Board Workflow Committee, Memorial Sloan-Kettering Cancer Center; 2004-2006.

Invited Participant, Joint NCI/British National Cancer Research Institute Gynecologic Cancer Intergroup Endometrial Cancer State-of-the-Science Meeting, Manchester, UK; November, 2006.

Member, Integration Panel, DOD Ovarian Cancer Research Program, 2001-2008.

Chair, Integration Panel, DOD Ovarian Cancer Research Program, 2005-2006.

Member, Peer Review Committee on Molecular Genetics and Oncogenes, American Cancer Society, 2002-2006.

Charter Member, Cancer Biomarkers Study Section, Center for Scientific Review, National Institutes of Health, 2003-2008.

Chair, Molecular and Cellular Biology and Genetics Peer Review Panel, Susan G. Komen for the Cure Grants Program; January, 2008.

Member, External Advisory Committee, SPORE in Ovarian Cancer, Fox Chase Cancer Center, Philadelphia, PA; 2003-2008.

Chair, Appointments and Promotions Committee, Anderson Cancer Institute, Memorial University Medical Center; 2006-2008.

Member, Board of Directors, Georgia Center for Oncology Research and Education; 2006-2008.

Member, Georgia Cancer Coalition Distinguished Cancer Scholar Review Committee; 2006-2008.

Chair, Medical Research Advisory Committee, Memorial University Medical Center; 2007-2008.

Member, Board of Advisors, College of Science and Technology, Georgia Southern University; 2006-2008.

Member, Special Emphasis Panel, NCI-ARRA P30 Biomedical Research Core Center Review, Rockville, MD; July, 2009.

Member, CDMRP Ovarian Cancer Grant Review Panel OC-4, Reston, VA; August, 2009.

Member, Scientific Advisory Committee, Ovarian Cancer Research Fund, 1999-2009.

Chair, DOD/CDMRP Breast Cancer Grant Review Panel MBG-B, Reston, VA; January, 2010.

Member, Scientific Review Group, NIH/NCI ZCA1 SRLB-R M1 R, Exceptional, Unconventional Research Enabling Knowledge Acceleration (EUREKA), Rockville, MD; March, 2010.

Member, Scientific Review Group, EDRN Biomarker Development Labs (U01), NIH/NCI ZCA1 SRLB-C M1 B, Bethesda, MD; May, 2010.

Chair, DOD/CDMRP Breast Cancer Research Program Grant Review Panel TRN-MBG, Reston, VA; May, 2010.

Chair, DOD/CDMRP Breast Cancer Research Program Grant Review Panel IDEA-MBG, Reston, VA; June, 2010.

Chairman, External Advisory Committee, SPORE in Ovarian Cancer, Dana-Farber/Harvard Cancer Center, Boston, MA; 2003-2010.

Member, Program Committee, 13th Biennial Meeting of the International Gynecologic Cancer Society, Prague, Czech Republic, 2010.

Member, Nominations Committee, Fox Chase Cancer Center, 2008-2010.

Member, Scientific Review Group, NIH/NCI ZCA1 SRLB-2 M1 R, Exceptional Unconventional Research Enabling Knowledge Acceleration (EUREKA), Bethesda, MD; March, 2011.

Member and Co-Chair, Subcommittee on Tissue Utilization, Gynecologic Oncology Group, 1997-2011.

Member, Scientific Review Group, NIH/NINR ZNR1 REV M 09, Personalized Genomics for Symptom Management: Bridging the Gaps from Genomic Discovery to Improved Health Outcomes, Bethesda, MD; June, 2011.

Member, Program Committee, Society for Gynecologic Oncology Annual Meeting, 2012.

Member, Board of Directors, Gynecologic Cancer Foundation (now Foundation for Women's Cancer); 2006-2013.

Member, Cancer Center Support Grant Executive Committee, Fox Chase Cancer Center, 2008-2013.

Member, President's Council, Fox Chase Cancer Center, 2008-2013.

Chair, DOD/CDMRP Breast Cancer Research Program Grant Review Panel BC12 TRN2, Reston, VA; February, 2013.

Member, Scientific Review Group, NCI ZCA1 RPRB-O (O1), NCI Small Grants Program for Cancer Research (NCI Omnibus R03), Reston, VA; June, 2013.

Member, Scientific Review Committee, DOD/CDMRP Ovarian Cancer Research Program Pilot Award Letter of Intent Review; July, 2013.

Chair, DOD/CDMRP Breast Cancer Research Program Grant Review Panel TRN2-CMB, Chantilly, VA; March, 2014.

Member, Executive Committee on Research, Fox Chase Cancer Center, 2008-2014.

Member, Scientific Review Committee, DOD/CDMRP Ovarian Cancer Research Program Pilot Award Letter of Intent Review; July, 2014.

Member, NCI Special Emphasis Panel for Review of Omnibus R21/R03 Applications in Response to PAR12-145/144; July, 2014.

Member, Scientific Review Committee, DOD/CDMRP Breast Cancer Research Program Grant Review Panel CBY-2, Reston, VA; July, 2014.

Member, Ovarian Cancer SPORE Executive Committee, Fox Chase Cancer Center, 2008-2015.

Founding Member, Genomic Advisory (Tumor) Board, Fox Chase Cancer Center, 2012-2015.

Member, Program Committee, Society of Gynecologic Oncology Annual Meeting, Chicago, IL; March, 2015.

Member, DOD/CDMRP Ovarian Cancer Research Program Pre-Application Review Panel, Pilot Award Mechanism; May-June, 2015.

Chair, DOD/CDMRP Breast Cancer Research Program Grant Review Panel, Molecular Biology and Genetics, Reston, VA; June, 2015.

Chair, Society of Gynecologic Oncology Genetics Delivery Care Summit, 2014-2015.

Invited Participant, Workshop on Ovarian Cancer, US Food and Drug Administration, White Oak, MD; July, 2015.

Member, Novartis Future of Diagnostic Laboratories Advisory Board, Austin, TX; November, 2015.

Invited Participant, Banbury Center Conference on, “Preventing BRCA-Related Cancer: a Think Tank for Innovative Strategies, Milestone Objectives, and Research Priorities”, Cold Spring Harbor, NY; November, 2015.

Member, Committee on Experimental Medicine, Gynecologic Oncology Group (now NRG Oncology), 1997-2014.

Co-Chair, Banbury Center Conference on, “After UKCTOCS: Public Messaging on Screening and Early Detection of Ovarian Cancer”, Cold Spring Harbor, NY; February, 2016.

Member, FORCE (Facing Our Risk of Cancer Empowered) Advisory Board; 2003-2013.

Member, Development Committee, Foundation for Women’s Cancer, 2013-2015.

Member, National Cancer Institute Special Emphasis Panel/Scientific Review Group 2016/05 ZCA1 PCRB-C (C2) B - Cell and Animal Models for Researching Disparities; February, 2016.

Chair, DOD/CDMRP Ovarian Cancer Research Program Grant Review Panel, Pathobiology Pilot Award Program; September, 2016.

Member, Clinical Practice Committee, Society of Gynecologic Oncology, 2014-2017.

Member, AACR Clinical and Translational Cancer Research Grants Scientific Review Committee, 2015-2017.

Member, National Cancer Institute Clinical Translational R21 and Omnibus R03 Special Emphasis Panel ZCA1 SRB-P (O1); May, 2018.

Member, Medical Student Interview Panel, Herbert Wertheim College of Medicine, Florida International University; 2017-2018.

Member, National Cancer Institute Special Emphasis Panel, ZCA1 SRB-P (J1) – Clinical and Translational Exploratory/Developmental Studies; September, 2018.

Co-Chair, Banbury Center Conference on, "Towards a Cure for Advanced Ovarian Cancer", Cold Spring Harbor, NY; October, 2018.

Member, Scientific Advisory Committee, Ovarian Cancer Research Alliance, 2001-2018.

Chair, Scientific Advisory Committee, Ovarian Cancer Research Alliance, 2009-2018.

Member, Board of Directors, Ovarian Cancer Research Fund Alliance, 2012-2018.

Member, Scientific Review Committee, National Cancer Institute Specialized Programs of Research Excellence II (P50); 2019/05 ZCA1 RPRB-7 (M1) P; January, 2019.

Member, Special Emphasis Panel-5, National Cancer Institute Clinical and Translational R21 and Omnibus R03; 2019/05 ZCA1 SRB-P (M2) S; January, 2019.

Committee Assignments (Current):

Member, External Advisory Board, SPORE in Ovarian Cancer, MD Anderson Cancer Center, Houston, TX; 2009-present.

Vice-Chair, Joint Scientific Advisory Committee, Stand Up to Cancer (SU2C) Ovarian Cancer Dream Team Grant; 2014-present.

Member, Cancer Education Committee: Cancer Prevention, Hereditary Genetics, and Epidemiology Track, American Society of Clinical Oncology (ASCO); 2016-present.

Member, Clinical Scientific Review Committee, Miami Cancer Institute, 2016-present.

Member, Board of Directors, Society of Gynecologic Oncology, 2017-2020.

Member, Medical Student Interview Panel, Herbert Wertheim College of Medicine, Florida International University; 2018-2019.

Member, Board of Directors, Florida International University Research Foundation; 2017-present.

Invited Lectures (Since 1992):

"Cell structure and tumor suppression" and "Molecular genetic techniques in human cancer research." South American Course in Cancer Research; Caracas, Venezuela; February, 1992.

"Form and function in molecular carcinogenesis." Third Frontiers in Science Symposium; NIH/NIEHS, Research Triangle Park, NC; April, 1992.

"Expression and function of the DCC gene in neural differentiation." Gordon Research Conference on Cancer; Newport, RI; August, 1992.

"DCC gene expression and function." Fifth Conference on Differentiation Therapy; Sardinia, Italy; September, 1992.

"Tumor suppressor genes I" and "Tumor suppressor genes II." Department of Toxicology, North Carolina State University, Raleigh, NC; September, 1992.

"Molecular genetics of human endometrial carcinoma." Department of Pathology, University of North Carolina, Chapel Hill, NC; September, 1992.

"Methods for the study of molecular genetics in human cancer." Department of Pathology, Jikei University School of Medicine, Tokyo, Japan; October, 1992.

"The role of cell structure in tumor suppression." Fourth International Conference of Anticancer Research; Crete, Greece; October, 1992.

"Molecular markers and endometrial cancer." Department of Epidemiology, University of North Carolina School of Public Health, Chapel Hill, NC; November, 1992.

"Tumor suppressor genes." Department of Epidemiology, University of North Carolina, Chapel Hill, NC; November, 1992.

"Role of cell and tissue structure in tumor suppression." Department of Pathology, Johns Hopkins University School of Medicine, Baltimore, MD; November, 1992.

"Endometrial hyperplasia and adenocarcinoma: Molecular genetic characterization and determinants of risk." American Association of Pathologists Annual Meeting; New Orleans, LA; March, 1993.

"The environment and women's health." First Annual Environmental Careers Symposium; NIH/NIEHS, Research Triangle Park, NC; May, 1993.

"Cell structure and tumor suppression." Gordon Research Conference on Biological Structure and Gene Expression; Volterra, Italy; May, 1993.

"Molecular genetics of human endometrial carcinoma." Department of Molecular and Cell Biology, University of California at Berkeley, Berkeley, CA; May, 1993.

"Molecular genetics of human endometrial carcinoma." Gordon Research Conference on Hormonal Carcinogenesis; Newport, RI; August, 1993.

"Molecular genetics of endometrial hyperplasia." Workshop on Alternatives to Hysterectomy, National Institutes of Health, Bethesda, MD; May, 1994.

"Molecular genetics of ovarian carcinoma." Third International Symposium on Ovarian Function, Sapporo, Japan; September, 1994.

"Molecular genetics of estrogen-associated cancers." Conference on Molecular Mechanisms of Environmental Carcinogenesis, Research Triangle Park, NC; September, 1994.

"Molecular genetics of gynecologic cancers." University of Pennsylvania Cancer Center Symposium on New Developments in Cancer Therapy: Focus on Gynecologic Cancers, Philadelphia, PA; December, 1994.

"Genetics and molecular medicine for the gynecologic oncologist", "BRCA1 and other genes involved in hereditary predisposition to reproductive cancer", Society of Gynecologic Oncologists Annual Meeting, San Francisco, CA; February, 1995.

"Hereditary Gynecologic Cancers." Grand Rounds, Department of Obstetrics and Gynecology, University of Pennsylvania Medical Center, Philadelphia, PA; March, 1995.

"Endometriosis and the Environment: Biomarkers of Toxin Exposure." Endometriosis 2000 Conference, National Institutes of Health, Bethesda, MD; May, 1995.

"Hereditary Gynecologic Cancers." Grand Rounds, Department of Obstetrics and Gynecology, Medical College of Pennsylvania, Philadelphia, PA; May 1995.

"E-Cadherin as a Tumor Suppressor." Gordon Research Conference on Cell Contact and Adhesion, Andover, NH; June, 1995.

"Mismatch Repair." American Urologic Association Summer Research Conference, Houston, TX; August, 1995.

“Genetic Characterization of Human Endometrial Carcinoma.” Ninth International Conference on Carcinogenesis and Risk Assessment, Austin, TX; November, 1995.

“Molecular Genetics of Ovarian Carcinoma.” The Finnish Medical Society Duodecim Annual Meeting, Turku, Finland; November, 1995.

“Hereditary Gynecologic Cancers.” Department of Pathology Grand Rounds, University of Pennsylvania Medical Center, Philadelphia, PA; November, 1995.

“Genetics of Hereditary Breast and Gynecologic Cancers.” Postgraduate Course on Molecular Biology of Gynecologic Cancers: Clinical Implications for the 1990s. Society of Gynecologic Oncologists Annual Meeting, New Orleans, LA; February, 1996.

“Molecular Genetics of Hereditary Gynecologic Cancers.” Department of Obstetrics and Gynecology Grand Rounds, Thomas Jefferson University, Philadelphia, PA; February, 1996.

“Hereditary Nonpolyposis Colorectal Cancer: Ethical, Legal, and Social Implications of Genetic Testing and Counseling for High Risk Individuals.” American Radium Society Annual Meeting, San Francisco, CA; March, 1996.

“Molecular Genetics of Hereditary Gynecologic Cancers.” Department of Genetics, University of Pennsylvania, Philadelphia, PA; May, 1996.

“Molecular Genetics of Hereditary Endometrial and Ovarian Carcinomas.” President’s Symposium of the New York Pathological Society, New York, NY; June, 1996.

“Familial Ovarian Cancer: Laboratory Diagnosis.” Current Concepts in Women’s Health Care: Seventeenth Annual Postgraduate Course, University of Pennsylvania Medical Center, Philadelphia, PA; June 1996.

“Molecular Genetics of Hereditary Gynecologic Cancers.” Barbara Moore Jordan Visiting Professorship, Memorial Sloan-Kettering Cancer Center, New York, NY; July 1996.

“Breast Cancer Genetics.” Keynote Lecture at the First Annual New Jersey Breast Cancer Research Symposium, Princeton, NJ; October, 1996.

“Estrogen as a Human Carcinogen: Molecular Genetics of Gynecologic Cancers.” US-Japan Cooperative Medical Science Program, Environmental Mutagenesis and Carcinogenesis Panel, Tokyo, Japan; November, 1996.

“Hereditary Breast and Ovarian Cancer: Molecular Genetics and Clinical Implications.” Grand Rounds, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY; December, 1996.

“Molecular Genetics of Hereditary Gynecologic Cancers.” Solid Tumor Oncology Conference, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY; February, 1997.

“Molecular Genetics of Hereditary Ovarian Cancer.” Basic Science Postgraduate Course; “BRCA1/2 and Other Genes Involved in Hereditary Predisposition to Ovarian Cancer.” Breakfast Session, Society of Gynecologic Oncologists Annual Meeting, Phoenix, AZ; March, 1997.

“Genetics of Ovarian Cancer.” Helene Harris Memorial Trust 6th International Forum on Ovarian Cancer, Los Angeles, CA; May, 1997.

“Genotype-Phenotype Correlations in Hereditary Ovarian Cancer.” Symposium on Ovarian Cancer: Prevention, Genetics and Treatment Challenges, Toronto, Ontario; May, 1997.

“Molecular Genetics of Hereditary Gynecologic Cancers.” Department of Pathology Grand Rounds, Memorial Sloan-Kettering Cancer Center, New York, NY; July, 1997. “Quantitative Methods in Cancer Genetics.”

Cancer Genetic Counseling and Testing: A Multidisciplinary Course, The Sarah Lawrence College Human Genetics Program, New York, NY; July, 1997.

“Hereditary Gynecologic Cancers: Molecular Genetics and Clinical Implications.” 26th Congress of Gynecologic Pathology and Colposcopy, Tokyo, Japan; July, 1997.

“Molecular Genetics of Estrogen-Associated Human Cancers.” Gordon Research Conference on Hormonal Carcinogenesis, Tilton, NH; July, 1997.

“Basic Principles of Genetics for Practicing Clinicians”, Genetic Techniques - Relevance for Practicing Clinicians”, and “Genetics of Gynecologic Sarcomas and Clinical Implications”. European School of Oncology Conference on Molecular Genetics in Gynecologic and Breast Cancer and Its Clinical Implications: Bridging the Gap, Budapest, Hungary; November, 1997.

“Studies on the Molecular Mechanism of Estrogen-Associated Human Cancers.” Department of Biochemistry, Mount Sinai University School of Medicine, New York, NY; November, 1997.

“Molecular Genetics of Hereditary Gynecologic and Breast Cancers.” Distinguished Lecturer in Oncology, University of Texas M.D. Anderson Cancer Center, Houston, TX; January, 1998.

“Genetics of Hereditary Gynecologic Cancers: What patients are asking their gynecologists.” Obstetrical Society of Philadelphia, Philadelphia, PA; February, 1998.

“Molecular Genetics of Hereditary Gynecologic Cancers.” Grand Rounds, Department of Obstetrics and Gynecology, Allegheny University of the Health Sciences, Philadelphia, PA; February, 1998.

“Endometrial Cancer.” Course on Human Genetics and Human Cancer, Memorial Sloan-Kettering Cancer Center, New York, NY; May, 1998.

“Molecular Genetics of Hereditary Gynecologic Cancers: Clinical Implications.” New York Gynecology Society, New York, NY; May, 1998.

“Hereditary Ovarian Cancer: Molecular Genetics and Clinical Implications.” IVth Sapporo International Symposium on Ovarian Function, Sapporo, Japan; August, 1998.

“Molecular Pathogenesis of Endometrial Neoplasia.” Grand Rounds, Department of Pathology, Brigham and Women’s Hospital, Boston, MA; October, 1998.

“Hereditary Gynecologic Cancers: Molecular Genetics and Clinical Implications.” Visiting Professor Program, Department of Pathology, Montefiore Medical Center, Bronx, NY; October, 1998.

“Molecular Genetics of Hereditary Gynecologic Cancers.” Memorial Hospital Annual Alumni Meeting, Memorial Sloan-Kettering Cancer Center, New York, NY; November, 1998.

“Clinical and Pathologic Features of BRCA-Associated Hereditary Ovarian Cancers.” Grand Rounds, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY; November, 1998.

“Genetic Epidemiology of Ovarian Cancer.” International Conference on Ovarian Cancer, The University of Texas M.D. Anderson Cancer Center, Houston, TX; February, 1999.

“Ovarian Cancer.” Course on Human Genetics and Human Cancer, Memorial Sloan-Kettering Cancer Center, New York, NY; April, 1999.

“Genetics of Ovarian Cancer.” Annual Conference of the National Corporate Medical Associates, Memorial Sloan-Kettering Cancer Center, New York, NY; June, 1999.

"Molecular Genetics of Hereditary Gynecologic Cancers." Scientific Symposium for Semi-Annual Business meeting of the Gynecologic Oncology Group, Scottsdale, AZ; July, 1999.

"Genetics." Breast Cancer Core Course, Memorial Sloan-Kettering Cancer Center, New York, NY; July, 1999.

"Genetic Susceptibility to Gynecologic Cancers." Cancer Smart Lecture Series, Memorial Sloan-Kettering Cancer Center, New York, NY; October, 1999.

"Molecular Genetics of Hereditary Breast Cancer: Clinical Implications." New York Pathological Society, New York, NY; February, 2000.

"Genetics of Hereditary Gynecologic Cancers." Postgraduate Course at the Society of Gynecologic Oncologists Annual Meeting, San Diego, CA; February, 2000.

"Molecular Genetics of Breast and Gynecologic Cancers." Course on Molecular Oncology, New York University School of Medicine, New York, NY; March, 2000.

Session Chair, Conference on Gynecologic Care of the Cancer Patient, Memorial Sloan-Kettering Cancer Center, New York, NY; March, 2000.

"Molecular Genetic Mechanism of Estrogen-Associated Human Tumorigenesis." Memorial Sloan-Kettering Cancer Center Scientific Retreat, March, 2000.

"Biology of Ovarian Cancer." Disease Management Team Conference Series (Gynecology), Memorial Sloan-Kettering Cancer Center, New York, NY; March, 2000.

"Preclinical Molecular Genetic Alterations in Breast and Ovarian Epithelium of BRCA Heterozygotes." American College of Surgeons Oncology Group Planning Conference. Memorial Sloan-Kettering Cancer Center; April, 2000.

Session Chair, Molecular Biology of Gynecologic Cancers, American Association for Cancer Research Annual Meeting, San Francisco, CA; April, 2000.

"Genetics of Hereditary Ovarian Cancer." Education Session on Ovarian Cancer, American Society of Clinical Oncology Annual Meeting, New Orleans, LA; May, 2000.

"Genetic Analysis of Ovarian Carcinoma Histogenesis." Ovarian Cancer National Alliance Third Annual Advocacy Conference, Washington, DC; September, 2000.

"Genetics of Cancer." Grand Rounds, Department of Medicine, Mercy Medical Center, Rockville Centre, NY; October, 2000.

"Can Molecular Markers Improve Risk Factor Determinations and Thereby Dictate Treatment and Improve Survival?", Plenary Session on Endometrial Cancer, VIII Meeting of the International Gynecologic Cancer Society, Buenos Aires, Argentina; October, 2000.

"Hereditary Ovarian Cancer: What We Know." Helene Harris Memorial Trust 8th International Forum on Ovarian Cancer, Houston, TX; March, 2001.

"Genetic Analysis of Ovarian Carcinoma Histogenesis." Gusberg Distinguished Lectureship in Gynecologic Oncology, Mt. Sinai Medical Center, New York, NY; April, 2001.

"Breast and Ovarian Cancers: Basic Science." A Comprehensive Review of Clinical Cancer Genetics, American Society of Clinical Oncology Annual Meeting, San Francisco, CA; May, 2001.

"Molecular Genetics of Hereditary Gynecologic and Breast Cancers: Clinical Implications." Grand Rounds, Department of Medicine, St. Clare's Medical Center, NJ; May, 2001.

"Molecular Biology of Gynecologic Cancers: Clinical Applications." Speaker of the Royal College of Physicians and Surgeons of Canada, Society of Gynecologic Oncologists of Canada Annual Meeting, St. John's, Newfoundland, Canada; June, 2001.

"Molecular Genetics of Hereditary Ovarian Cancer: Clinical Applications." Canadian Federation of Biological Sciences Annual Meeting, Ottawa, Canada; June, 2001.

"Molecular Genetics of Hereditary Ovarian Cancer: Translational Applications." NCI/Center for Cancer Research Grand Rounds, Bethesda, MD; July, 2001.

"Molecular Genetics of Hereditary Gynecologic Cancers: Clinical Implications. Grand Rounds, Department of Obstetrics and Gynecology, Long Island Hospital, Brooklyn, NY; October, 2001.

"Can Clinical Problems in Ovarian Cancer be Solved in the Laboratory?" Visiting Professorship, Department of Obstetrics and Gynaecology, University of Toronto, Toronto, Canada; October, 2001.

"Molecular Genetics of Hereditary Gynecologic and Breast Cancers: Clinical Implications." Grand Rounds, Department of Obstetrics and Gynecology, Columbia University, New York; March, 2002.

“Molecular Genetics of Hereditary Gynecologic Cancers.” Postgraduate Course of Clinical Usefulness of Genetic Testing in Gynecologic Oncology. Society of Gynecologic Oncologists Annual Meeting, Miami Beach, FL; March, 2002.

“Cancer Genetics.” Course on Molecular Oncology, New York University, New York; March, 2002.

“Genetic Analysis of Ovarian Carcinoma Histogenesis.” Conference on Ovarian Cancer and High-Risk Women: Implications of Screening, Prevention, and Early Detection, University of Pittsburgh, Magee-Women’s Hospital, Pittsburgh, PA; May, 2002.

“Basic Science of Breast and Ovarian Cancer.” Comprehensive Course on Clinical Cancer Genetics, American Society of Clinical Oncology Annual Meeting, Orlando, FL, May, 2002.

“Toward a Molecular Classification of Endometrial Carcinoma.” Education Session on Endometrial Carcinoma, American Society of Clinical Oncology Annual Meeting, Orlando, FL; May, 2002.

“Hereditary Gynecologic Cancers: Clinical Implications.” National Corporate Medical Associates Annual Meeting, Memorial Sloan-Kettering Cancer Center, New York, NY; June, 2002.

“Molecular Genetics of Hereditary Ovarian Cancer.” Third Annual International Conference on Ovarian Cancer, MD Anderson Cancer Center, Houston, TX; September, 2002.

“Molecular Biology of Ovarian Cancer: From Pathogenesis to Treatment.” Symposium on Ovarian Cancer, International Gynecologic Cancer Society Biennial Meeting, Seoul, Korea; October, 2002.

“Histogenesis of Ovarian Cancer.” The Ethel N. Ruvelson Lecture in Ovarian Cancer, 33rd Annual Autumn Seminar in Obstetrics and Gynecology, University of Minnesota, Minneapolis, MN; October, 2002.

“Hereditary Gynecologic Cancers: What We Know.” Society of Gynecologic Oncologists Winter Meeting, Breckenridge, CO; March, 2003.

“Genetic Analysis of Ovarian Carcinoma Histogenesis.” Helene Harris Memorial Trust 9th Biennial Forum on Ovarian Cancer, Stratford-upon-Avon, United Kingdom; March, 2003.

“Cáncer de Ovario: Historia Natural y Biología Molecular.” Cánceres de Próstata, Mama y Ovario: Tumores Hormono-Dependientes, Universidad Internacional Menéndez Pelayo, Santander, Spain; July, 2003.

“Gynecologic Tumors.” Session on New Directions in Cancer, AACR Annual Meeting, Washington, DC; July, 2003.

“Molecular Genetics of Hereditary Gynecologic and Breast Cancers: Clinical Implications.” Hoag Cancer Center Grand Rounds, Newport Beach, CA; July, 2003.

“Genetic Analysis of Ovarian Carcinoma Histogenesis.” Grand Rounds, Department of Pathology, Yale-New Haven Hospital, New Haven, CT; September, 2003.

“Gene Silencing by Estrogen Receptor-Dependent Promoter Methylation.” e.hormone 2003, 5th Annual Conference on Environmental Estrogens. Tulane University, New Orleans, LA; October, 2003.

“Genetics of Hereditary Breast and Gynecologic Cancers: Clinical Implications.” 5th Annual Kimmel Cancer Center Hereditary Cancer Conference. Thomas Jefferson University, Philadelphia, PA; November, 2003.

Distinguished Visiting Professorship. “Genetic Analysis of Ovarian Carcinoma Histogenesis. Department of Pathology, Johns Hopkins University, Baltimore, MD; November, 2003.

“Genetic Analysis of Ovarian Carcinoma Histogenesis.” 19th Annual Ella T. Grasso Memorial Conference. University of Connecticut Health Center, Hartford, CT; November, 2003.

The 13th Annual Per Kolstad Memorial Lecture. “Genetics of Hereditary Ovarian Cancer: Clinical Implications.” The Norwegian Radium Hospital, Oslo, Norway; December, 2003.

“Genetic Analysis of Ovarian Carcinoma Histogenesis.” Medical Oncology and Ovarian Cancer Research Program Seminar Series, Fox Chase Cancer Center, Philadelphia, PA; January, 2004.

“BRCA - A Paradigm for Hereditary Cancer Predisposition.” Postgraduate Course on “Genetics for Gynecologic Oncologists”, Society for Gynecologic Oncologists Annual Meeting, San Diego, CA; February, 2004.

“Role of Gene Expression Profiling in Distinguishing Biologically and Clinically Distinct Subclasses of Endometrial Carcinoma.” Gynecologic Cancer Models, Mouse Models of Human Cancers Consortium (NCI) Meeting, San Juan, Puerto Rico; February, 2004.

“Human Cancer Genetics.” Course on Molecular Oncology, New York University, New York, NY; February, 2004.

“Genetic Analysis of Ovarian Carcinoma Histogenesis.” Mayo Oncology Society, Rochester, MN; March, 2004.

“Ovarian Cancer - New Concepts in Organ-Site Research.” American Association for Cancer Research Annual Meeting, Orlando, FL; March, 2004.

“Insights into Biology and Clinical Behavior of Endometrial Carcinoma through Comprehensive Gene Expression Profiling.” Symposium on Ovarian Cancer and Other Gynecologic Malignancies, New York, NY; April, 2004.

“Genetics of Hereditary Gynecologic Cancers.” American Society of Clinical Oncology Annual Meeting, ASCO/SGO Special Session on Clinical Management of Patients with Hereditary Predisposition to Gynecologic Cancers, New Orleans, LA; June, 2004.

“Gene Silencing through Estrogen Receptor Mediated Promoter Methylation.” Gordon Research Conference on Reproductive Tract Biology, New London, CT; June, 2004.

“Genetic Analysis of Ovarian Carcinoma Histogenesis.” Third Early Detection Research Network Scientific Workshop, Bethesda, MD; June, 2004.

“Stratification of Intermediate Risk Disease by Gene Expression Profiling.” 2nd Annual Uterine Cancer Biology Symposium, MD Anderson Cancer Center, Houston, TX; September, 2004.

“Is There a Molecular Basis for the Developmental Estrogenization Syndrome?” e.hormone 2004 Conference, New Orleans, LA; October, 2004.

“Genetic Analysis of Ovarian Carcinoma Histogenesis.” Grand Rounds, Dana-Farber/Massachusetts General Hospital, Boston, MA; November, 2004.

“Genetic Analysis of Ovarian Carcinoma Histogenesis.” Grand Rounds, Curtis and Elizabeth Anderson Cancer Institute at Memorial Health University Medical Center, Savannah, GA; December, 2004.

Chair, “Postgraduate Course on Molecular Biology for Gynecologic Oncologists.” Society for Gynecologic Oncologists Annual Meeting, Miami Beach, FL; March, 2005.

“Genetics of the Early Natural History of Ovarian Cancer.” Helene Harris Memorial Trust 10th Annual Biennial International Forum on Ovarian Cancer, Washington, DC; April, 2005.

“Genetic Analysis of Ovarian Carcinoma Histogenesis.” Elkin Cancer Biology Seminar Series, Winship Cancer Institute, Emory University School of Medicine, Atlanta, GA; March, 2005.

“Microarray Technology in Gynecologic Cancer Research.” 2nd International Symposium on Ovarian Cancer and Other Gynecologic Malignancies, New York, NY; April, 2005.

“Hereditary Ovarian Cancer.” Postgraduate Course on Gynecologic Cancer 2005, Medical College of Georgia/Curtis and Elizabeth Anderson Cancer Institute, Savannah, GA; April, 2005.

“Role of Defective DNA Repair in Gynecologic Tumorigenesis.” Lynne Cohen Symposium on the Emerging Role of Screening and Prevention in Women’s Cancers, NYU University School of Medicine, New York, NY; April, 2005.

“Genetic Analysis of Ovarian Carcinoma Histogenesis.” Multidisciplinary International Conference on Gynecologic Cancer, Bologna, Italy; June, 2005.

“Gene Silencing through Estrogen Receptor-Mediated Promoter Hypermethylation.” Biomedical Research Seminar Program, Mercer University School of Medicine, Macon GA; September, 2005.

“Treatment of Hereditary Ovarian Cancer: Clinical and Experimental Approaches.” And “Haploinsufficiency: Is it Important?” International Symposium on *BRCA*: Today and Tomorrow, Montréal, Canada; October, 2005.

“Opening Key Note Address: Genetic Analysis of Ovarian Carcinoma Histogenesis.” Symposium on Ovarian Cancer: Prevention and Detection of the Disease and its Recurrence. University of Pittsburgh Cancer Institute, Pittsburgh, PA; October, 2005.

“Genetic Analysis of Ovarian Carcinoma Histogenesis.” Grand Rounds, Department of Pathology and Laboratory Medicine, MD Anderson Cancer Center, Houston, TX; January, 2006.

“Cancer Genetics.” Course on Molecular Oncology, New York University School of Medicine, New York, NY; March, 2006.

“Genome-Based Laboratory Approaches to Advancing the Practice of Gynecologic Oncology.” Postgraduate Course on Translational Research, Society for Gynecologic Oncologists Annual Meeting, Palm Springs, CA; March, 2006.

“Translational Research.” Memorial Health University Medical Center First Resident Alumni CME Program, Savannah, GA; June, 2006.

“Molecular Medicine.” Department of Internal Medicine, Memorial Health University Medical Center, Savannah, GA; August, 2006.

“Molecular Basis of Improved Survival in *BRCA*-Linked Ovarian Cancers.” 11th Biennial Meeting of the International Gynecologic Cancer Society, Santa Monica, CA; October, 2006.

“Genetic Analysis of Ovarian Carcinoma Histogenesis.” Winter Symposium, Department of Obstetrics and Gynecology, Rambam Health Care Campus, Haifa, Israel; January, 2007.

“Functional Analysis of the CA125 (MUC16) Gene Product in Ovarian Tumorigenesis.” Helene Harris Memorial Trust 11th Biennial International Forum on Ovarian Cancer, Lake Como, Italy; March, 2007.

Discussant, Focused Plenary Session on Translational Research in Ovarian Cancer. Society of Gynecologic Oncologists Annual Meeting, San Diego, CA; March, 2007.

“Innovative Cancer Research Activities in Georgia.” Georgia Cancer Summit, Atlanta, GA; January, 2008.

“Applications of Genomics/Proteomics Technologies to Gynecologic Cancers?” Gynecologic Oncology Group Scientific Session on “Genomics and Proteomics: The Future is Now”. GOG Semi-Annual Meeting, San Diego, CA; January, 2008.

“Molecular Evolution of Ovarian Cancer.” 1st Ovarian Cancer Action International Conference, London, United Kingdom; March, 2008.

“Genetics 101.” Sunrise Postgraduate Session, Society of Gynecologic Oncologists Annual Meeting, Tampa, FL; March, 2008.

Discussant, Focused Plenary Session on Translational Research, Society of Gynecologic Oncologists Annual Meeting, Tampa, FL; March, 2008.

“Genetic Profiling of Endometrial Cancers.” Fifth International Symposium on Ovarian Cancer and Gynecologic Malignancies, New York, NY; March, 2008.

“Cancer Genetics.” Grand Rounds, Department of Internal Medicine, Memorial University Medical Center, Savannah, GA; April, 2008.

“The Future of Healthcare: Genetic Medicine.” Annual Meeting of the Coastal Empire Health Underwriters Association, Savannah, GA; May, 2008.

“Relevance of Tumor Biology to Prevention and Diagnosis.” International Symposium on Hereditary Breast and Ovarian Cancer: Risks and Challenges, Bari, Italy; September, 2009.

“Whence Epithelial Ovarian Carcinoma?” Robert F. Ozols Symposium on Gyn Cancer: Gyn Cancers – the Next 25 Years, Philadelphia, PA; September, 2009.

Session Chair. Opening Plenary Session I; Interactive Session: “Hereditary Gynecologic Cancers.” 13th Biennial Meeting of the International Gynecologic Cancer Society, Prague, Czech Republic; October, 2010.

“Whence Epithelial Ovarian Carcinoma?” Ovarian Cancer National Alliance Regional Symposium; Radnor, PA; November, 2010.

“The Origin of Epithelial Ovarian Carcinoma: New Insights.” Omniprex 2011 Ovarian Cancer Course; Philadelphia, PA; April, 2011.

“Whence Epithelial Ovarian Carcinoma?” Grand Rounds, Department of Obstetrics and Gynecology, Michigan State University School of Medicine; Grand Rapids, MI; May, 2011.

“Low Grade Serous Carcinomas.” From Molecular Information to Cancer Medicine - NCI Translational Science Meeting 2011, Washington, DC; July, 2011.

“The Vision and the Reality: One Cancer Center’s Journey toward Genomic Medicine.” Keynote Session, The Clinical Genome Conference, San Francisco, CA; June, 2012.

“The Vision and the Reality: One Cancer Center’s Journey toward Genomic Medicine.” Keynote Session, Ion Torrent User’s Group Meeting, Baltimore, MD; March, 2013.

“Cancer Genetics and the Evolution of Precision Medicine.” Memorial Sloan-Kettering Cancer Center, New York, NY; May, 2013.

Co-Organizer, “Ovarian Cancer: Developing Research-Based Public Messaging on Early Detection and Screening.” The Banbury Center, Cold Spring Harbor, NY; October, 2013.

“Cancer Genetics and the Evolution of Precision Medicine.” Grand Rounds, Department of Obstetrics and Gynecology, New York University School of Medicine, New York, NY; February, 2014.

“Defective Homologous Recombination and Therapeutic Opportunities in Ovarian Cancer.” First Annual Meeting of International Ovarian Cancer Consortium: Tumor Microenvironment and Drug Discovery, University of Oklahoma Health Sciences Center, Oklahoma City, OK; February, 2014.

“Ethical, Legal, and Social Implications of Clinical Next-Generation Sequencing.” Cancer Prevention and Control Program, Fox Chase Cancer Center, Philadelphia, PA; March, 2014.

“Lecturette: The Use of “omics”-Based Predictors in Clinical and Translational Research.” Society of Gynecologic Oncology Annual Meeting, Tampa, FL; March, 2014.

“Genetic Solutions to the Cancer Problem: A Personal Perspective.” The Jackson Laboratory for Genomic Medicine, Farmington, CT; August, 2014.

Keynote Presentation: “The Vision and the Reality: One Cancer Center’s Journey toward Genomic Medicine.” Seventh Annual Predictive Cancer Biomarkers Conference, Washington, DC; August, 2014.

“The Vision and the Reality: One Cancer Center’s Journey toward Genomic Medicine.” Third Annual Genomics in Medicine Symposium – Molecular Medicine Tri-Conference 2015, San Francisco, CA; February, 2015.

Panel Member, “Targeted Oncology”. BIO 2015 International Conference, Philadelphia, PA; June, 2015.

“The Vision and the Reality: One Cancer Center’s Journey toward Genomic Medicine.” 8th Annual Predictive Cancer Biomarkers Conference, Washington, DC; August, 2015.

“Cancer Genetics and the Evolution of Precision Medicine.” Grand Rounds, Broward Health Medical Center, Ft. Lauderdale, FL; March, 2016.

“Genetics of Women’s Cancers: Advances through Genomic Medicine.” Fifth Annual Omar Pasalodos, MD, Memorial Lecture, Miami, FL; April, 2016.

“Advances in Genomic Medicine: Focus on Head and Neck Cancers.” Fifth Annual Head and Neck Cancer Symposium, Miami, FL; April, 2016.

“Cancer Genetics in the Primary Care Setting.” The International Symposium on Primary Care, Miami Beach, FL; July, 2016.

“Genomic Predisposition to Breast Cancer.” Fourth Annual John M. Cassel, MD, Memorial Breast Cancer Symposium, Miami, FL; September, 2016.

“Updates on the UKCTOCS Trial.” Ovarian Cancer State-of-the-Art Conference, Memorial Sloan-Kettering Cancer Center, New York, NY; October, 2016.

“Genetics of Cancer: New Opportunities through Genomic Medicine.” Miami Medical Forum, Miami, FL; October, 2016.

“Cancer Genetics and the Evolution of Precision Medicine.” Presidential Plenary Session, International Gynecologic Cancer Society Biennial Meeting, Lisbon, Portugal; October, 2016.

“Genetic Predisposition to Cancer.” Baptist Health South Florida Research Summit: Bringing Cancer Research to the Community, Miami, FL; November, 2016.

“Germline Testing Meets Genomic Testing: How to Sort It Out.” Second Annual West Cancer Center Oncology Conference: Collaboration for the Future Cure: Precision Medicine and Immuno-Oncology, Memphis, TN; November, 2016.

“Genetics of Women’s Cancers: Advances through Genomic Medicine.” Second Annual MSK Cancer Alliance Scientific Symposium, Miami, FL; January, 2017.

“Precision Medicine in Cancer Care: Global Challenges and Opportunities.” Enmore Bio Conference, Nanjing, China; February, 2017.

“Genetics of Women’s Cancers: Advances through Genomic Medicine.” Grand Rounds, Department of Obstetrics and Gynecology, Lehigh Valley Health Network, Allentown, PA; May, 2017.

“How to Interpret Tumor Genomics for the Oncologist.” Education Session on Cascade Testing: What to Do When Ascertaining Germline Mutations from Tumor and Other Genomic Testing. American Society of Clinical Oncology Annual Meeting, Chicago, IL; June, 2017.

“Genetics of Women’s Cancers: Advances through Genomic Medicine.” President’s Guest Speaker, Miami Obstetrical and Gynecological Society, Miami, FL; September, 2017.

“Genetics of Women’s Cancers: Advances through Genomic Medicine.” Grand Rounds, Simon Cancer Center, Indiana University, Indianapolis, IN; October, 2017.

“Genomics and Pediatric Malignancies.” Kids with Cancer Symposium, Miami, FL; December, 2017.

“The Challenges and Rewards for Bringing AI into the Clinic for Health and Disease Management.” Panel Discussion, Precision Medicine World Conference, Mountain View, CA; January, 2018.

“Genomics Revolution in Cancer Care.” Al and Janie Nahmad Speaker Series: Thought Leaders in Medicine, Miami, FL; April, 2018.

“Cancer Genomics.” Baptist Health International Videoconference, Miami, FL; September, 2018.

“Estrogen and Cancer.” Visiting Professorship, Department of Obstetrics and Gynecology, University of Chicago, Chicago, IL; September, 2018.

“BRCA, Genetics, and Genomics: Role in Ovarian Cancer.” Fight N Heal Teal Symposium, Miami, FL; October, 2018.

Ad Hoc Reviewer:

American Journal of Human Genetics	Journal of Experimental Medicine
American Journal of Obstet and Gynecol	Journal of Medical Genetics
American Journal of Pathology	Journal of Molecular Diagnostics
Annals of Surgical Oncology	Journal of Molecular Endocrinology
BBA Reviews on Cancer	Journal of the National Cancer Inst
BMC Cancer	Lancet
Breast Cancer Research and Treatment	Molecular Cancer Therapeutics
British Journal of Cancer	Molecular Carcinogenesis
Cancer	Molecular Endocrinology
Cancer Biology and Therapy	Molecular Pharmacology
Cancer Research	Nature
Clinical Cancer Research	Nature Communications
Endocrinology	Nature Genetics
European Journal of Cancer	Nature Medicine
Genes, Chromosomes, and Cancer	Nature Reviews Cancer
Genomics	New England Journal of Medicine
Gynecologic Oncology	Nucleic Acids Research
International Journal of Cancer	Obstetrics and Gynecology
International Journal of Gynecologic Cancer	Oncogene
International Journal of Oncology	Proc Natl Acad Sci USA
Journal of the American Medical Association	Science
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	The Oncologist

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EXHIBIT B

Testifying History for Jeff Boyd, Ph.D.

**University of Miami v. Agency for Health Care Administration and Baptist
Hospital of Miami, Inc.**

State of Florida Division of Administrative Hearings
Case No. 16-001698CON

**University of Miami v. Baptist Hospital of Miami, Inc., and Agency for Health
Care Administration**

State of Florida Division of Administrative Hearings
Case No. 17-005301CON